# Impact of the Saskatchewan Seniors' Drug Plan (SDP) to Medication Utilization and Adherence among Saskatchewan Residents

A Thesis Submitted to the College of Graduate Studies and Research for the Degree of Master's of Science in the College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon

By

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## Abstract

**Background:**

In 2007, Saskatchewan's Ministry of Health launched the Seniors' Drug Plan (SDP), whereby provincial beneficiaries at or above the age of 65 receive medications at a maximum self-payment of $15. The purpose of this study was to document the impact of the SDP using provincial health-administrative databases.

**Methods:**

Aggregate medication utilization and costs were described using the prescription drug database starting two years before the implementation of the SDP and continuing for two years after. Interrupted time series analysis using segmented regression models were developed to test the impact of the SDP. Also, the probability of achieving optimal medication adherence was examined among cohorts receiving medications after SDP implementation versus similar patients receiving medications before the SDP and also a group of patients <65 years who were not eligible for the SDP at all. The impact of the SDP on the outcome of optimal adherence was estimated using logistic regression models with generalized estimating equations (GEE).

**Results:**

Monthly government spending on medications increased by 47.5% following implementation of the SDP, while total medication dispensations only increased by 5.8%. The SDP was associated with more dispensations per month among prevalent users (+5.4%, 95% CI: 1.3% to 9.5%) but not incident users who did not receive the study medication in the previous 365 days (+1.3%, 95% CI: -8.0% to 10.7%).

Similarly, the SDP did not appear to impact the use of blood-glucose-lowering agents, (-0.5%, 95% CI: -6.2% to 5.2%). A small but significant increase in the odds of optimal medication adherence was observed after the SDP compared with before (OR=1.08, 95% CI 1.04 to 1.11). However, the impact was only observed in prevalent users (OR=1.08, 95% CI 1.04 to 1.12), but not incident users (OR=1.05, 95% CI 0.98 to 1.13). Also, the impact of the SDP on medication adherence was not consistent for all medication classes examined.

**Discussion:**

In summary, the SDP resulted in substantially higher government investment into drug costs without a major effect on medication utilization and adherence. However, cost reduction for seniors must have provided substantial relief independent of the impact on adherence and utilization.

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## Table of Contents

# List of Tables

## Chapter 2



## Chapter 3



## Chapter 4

# List of Figures

## Chapter 2



## Chapter 3

**Chapter 4**

## List of Acronyms

| | |
|---|---|
| 95% CI | 95% Confidence Interval |
| ACEI | Angiotensin-Converting-Enzyme Inhibitor |
| AHFS | American Hospital Formulary Service |
| AIC | Akaike Information Criterion |
| ARB | Angiotensin Receptor Blocker |
| CCB | Calcium Channel Blocker |
| CCI | Charlson Comorbidity Index |
| COX-2 | Cyclooxygenase-2 |
| DAD | Discharge Abstract Database |
| DHP | Dihydropyridine |
| DIN | Drug Identification Number |
| DSA | Data Sharing Agreement |
| EENT | Eye, Ear, Nose, and Throat |
| GDP | Gross Domestic Product |
| GEE | Generalized Estimating Equations |
| HQC | Health Quality Council |
| ICD | International Classification of Disease |
| MDD | Major Depress Disorders |
| MSB | Medical Services Branch (database) |
| MEMS® | Medication Event Monitoring System |
| MPR | Medication Possession Ratio |
| OOP | Out-Of-Pocket |
| OR | Odds Ratio |
| OTC | Over-The-Counter |
| PDP | Prescription Drug Plan |
| PIM | Potential Inappropriate Medication |
| PRS | Person Registry System |

| | |
|---|---|
| QIC | Quasi-Akaike Information Criterion |
| RCT | Randomized Control Trials |
| SDP | Seniors' Drug Plan |
| SDS | Sheehan Disability Scale |
| SNRI | Serotonin-Norepinephrine Reuptake Inhibitor |
| SSRI | Selective Serotonin Reuptake Inhibitor |
| VBID | Value Based Insurance Designs |
| WHO | World Health Organization |

# Chapter 1 Introduction

Chronic diseases place an enormous strain on Canada's health care system and the national economy.(1) Spending on medications for chronic diseases is now the second largest contributor to total health care spending in Canada and is increasing dramatically.(1) Conditions such as cardiovascular diseases, diabetes, and depression are particularly important in this regard because of their heavy reliance on chronic medications.(2) Although medications for these conditions have proven to reduce expensive and life threatening outcomes, approximately 50% of individuals with cardiovascular conditions, diabetes, or depression do not take prescribed chronic medications regularly.(3) This phenomenon is described as medication non-adherence.(4)

Medication cost may be an important barrier to achieving ongoing medication adherence for patients;(65–69) it may also be a possible target for improving medication adherence at the population level.(68) Ultimately, improvements in medication adherence can result in more successful management of chronic diseases in the community, allowing patients to reduce their need for hospitalization.(68, 163–167)

On July 1st, 2007, the Saskatchewan government launched the SDP to reduce seniors' (age 65 and over) out-of-pocket (OOP) costs to a maximum of $15 per prescription for all medications covered under the provincial drug formulary. The objectives of this study were: 1) to examine trends in the utilization of medications in Saskatchewan prior to, and following the implementation/modification of the SDP; and 2) to estimate the impact of the SDP on medication non-adherence for major chronic conditions in Saskatchewan.

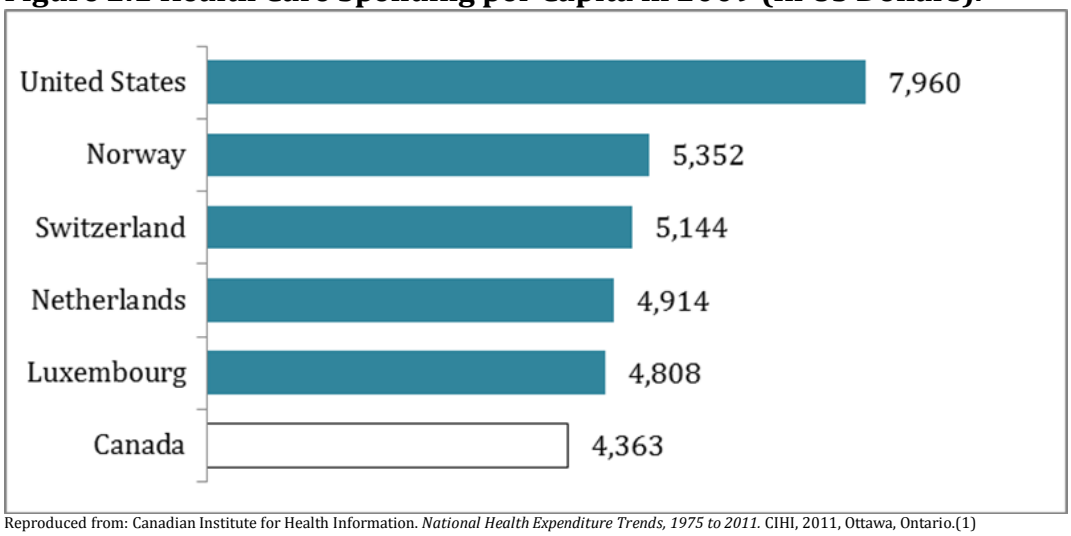
# Chapter 2 Literature Review

## 2.1 Chronic Diseases and Medication Use in Canada

Chronic diseases are defined by the World Health Organization (WHO) as "diseases of long duration and generally slow progression".(5) These conditions are common, costly, and life-threatening. It is estimated that almost 50% of Canadians (approximately 16 million) live with at least one chronic condition,(6) while 81% of those over the age of 65 are afflicted.(7) Furthermore, 33% of seniors have three or more chronic conditions concurrently.(7)

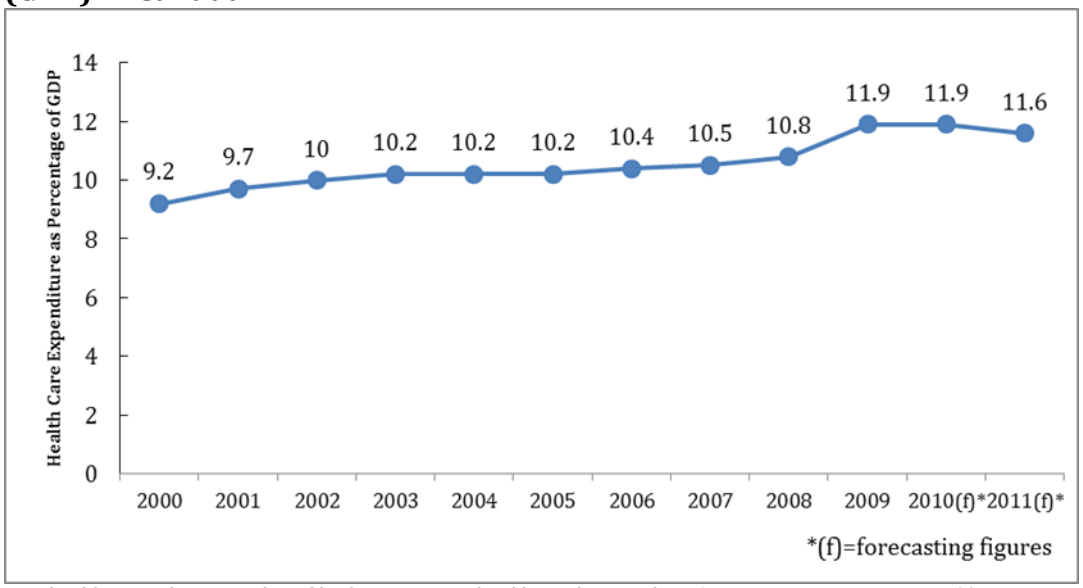
The high prevalence of chronic conditions places an enormous strain on Canada's health care system as well as the national economy. (1) In 2011, Canada spent approximately $5,811 per person on health care totaling $200.5 billion.(1) This level of spending ranked in the top six of developed countries on health care spending per capita (Figure 2.1). Healthcare spending represented 11.6% of Canada's Gross Domestic Product (GDP) in 2011 (Figure 2.2) and had grown an average of 4.5% annually since 1996.(1) Almost three quarters of total health spending (70% or $141 billion) is paid by Canadian governments while the rest is paid by individuals or private insurance providers.(1)

**Figure 2.1 Health Care Spending per Capita in 2009 (In US Dollars).**




Reproduced from: Canadian Institute for Health Information. *National Health Expenditure Trends, 1975 to 2011.* CIHI, 2011, Ottawa, Ontario.(1)

**Figure 2.2 Health Care Spending as Percentage of Gross Domestic Product (GDP) in Canada.**



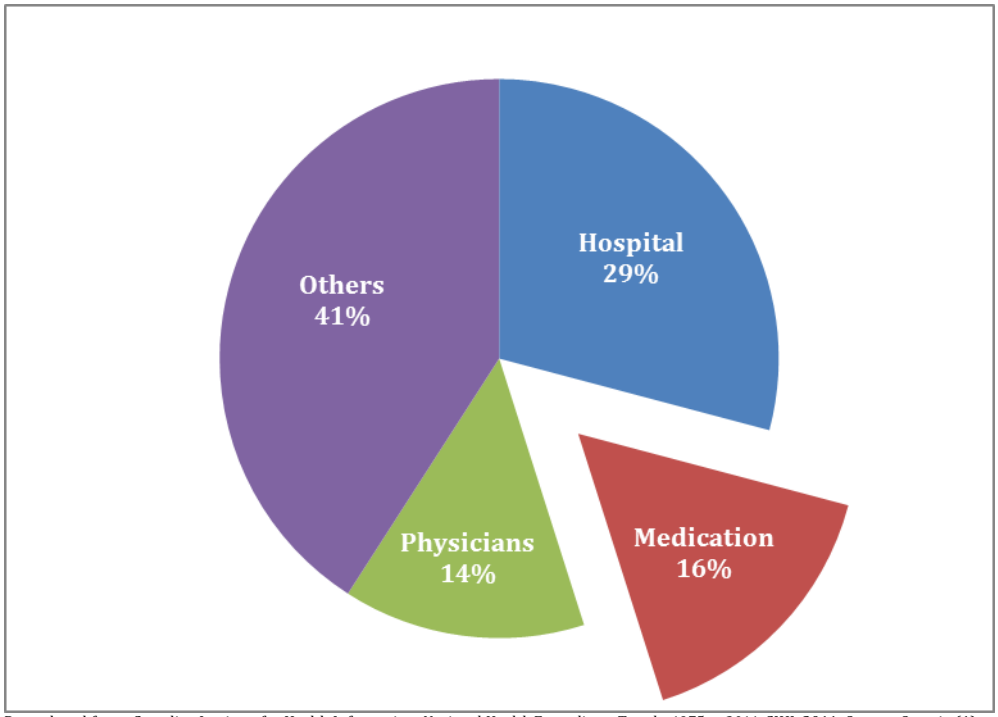

Reproduced from: Canadian Institute for Health Information. *National Health Expenditure Trends, 1975 to 2011.* CIHI, 2011, Ottawa, Ontario.(1)

Chronic diseases are responsible for a substantial portion of total health care costs in Canada.(8) They also consume non-health care dollars through their disabling effects to Canadians who would otherwise continue working and paying taxes. In 2005, almost 90% of deaths in Canada (207,000/231,000) could be

attributed to chronic diseases.(6,9) The resulting economic impact accounts for almost two thirds of the total costs due to loss of productivity from premature death or premature disability.(8)

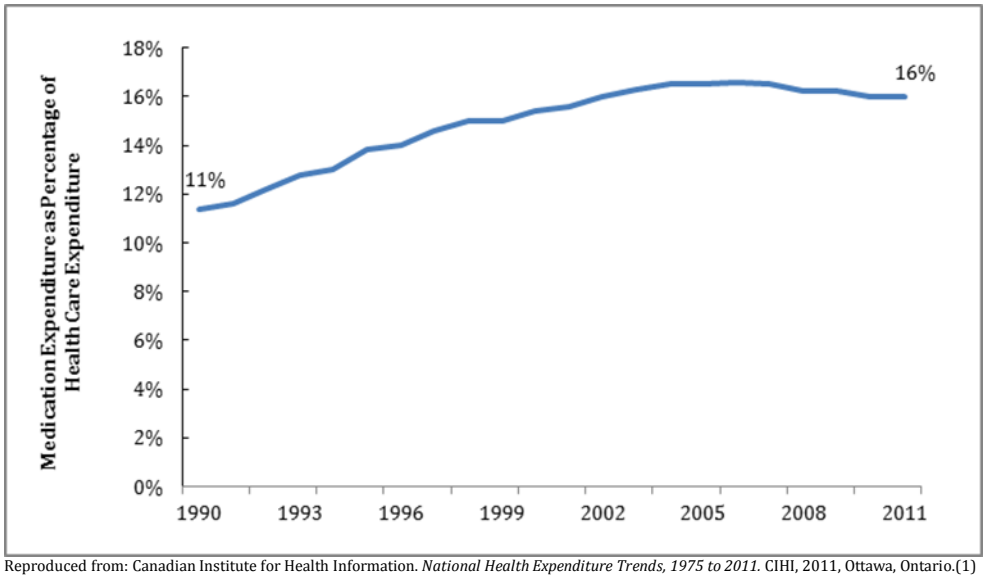
In Canada, spending on medications ($32 billion) was the second-largest component of health costs in 2011, second only to hospital services, as displayed in figure 2.3.(1) Medication costs increased from 11% to 16% (Figure 2.4) of Canada's total health expenditures between 1990 and 2011 and were the main driver of overall growth.(10) Table 2.1 shows the leading ten categories driving medication spending; the majority of these are used to manage chronic diseases.(10)

**Figure 2.3 Major Contributors to Health Care Spending in Canada in 2011.**




Reproduced from: Canadian Institute for Health Information. *National Health Expenditure Trends, 1975 to 2011.* CIHI, 2011, Ottawa, Ontario.(1)

**Figure 2.4 Trends in Medication Expenditure as Percentage of Health Care Cost in Canada.**




Reproduced from: Canadian Institute for Health Information. *National Health Expenditure Trends, 1975 to 2011.* CIHI, 2011, Ottawa, Ontario.(1)

**Table 2.1 Prescription Medications Associated with the Highest Spending Increases in Canada between 2005 and 2010.**

| Medication Class | Contribution to Growth (%) | Average Annual Growth (%) |
|---|---|---|
| Immunosuppressants | 12.2 | 25.1 |
| Cholesterol-lowering Drugs | 10.5 | 7.8 |
| Cancer Drugs | 9.3 | 13.4 |
| Respiratory Drugs | 5.4 | 8.4 |
| Diabetes Drugs | 4.5 | 9.9 |
| Analgesics | 4.3 | 6.3 |
| Anti-HIV(human immunodeficiency virus) Drugs | 4.1 | 11.4 |
| Antiepileptic Drugs | 3.5 | 13.0 |
| Antidepressants | 3.0 | 4.2 |
| Blood pressure lowering drugs | 2.7 | 1.6 |

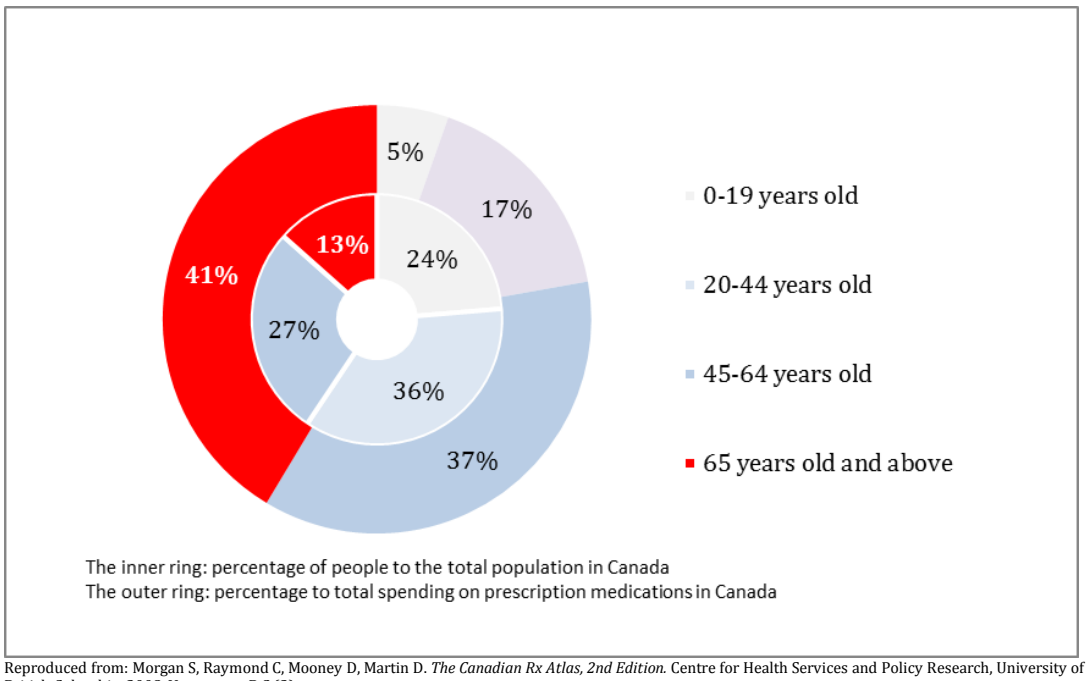
Reproduced from: Canadian Institute for Health Information. *Drivers of Prescription Drug Spending in Canada.* CIHI, 2012, Ottawa, Ontario.(10)

A few highly prevalent chronic conditions, including cardiovascular diseases (e.g., high blood pressure, heart disease, and stroke), diabetes, and depression contribute disproportionately to overall health care costs.(11) Almost half of

Canadian seniors at or above the age of 65 years have high blood pressure (47% or 2 million), 24% have heart disease or stroke, 17% have diabetes, and 8% have depression.(11) The direct cost of cardiovascular diseases, including heart disease and stroke, was estimated at $7.6 billion in 2000,(12) while the direct costs of mental illness (including depression) were estimated at $4.9 billion in 2003.(13)

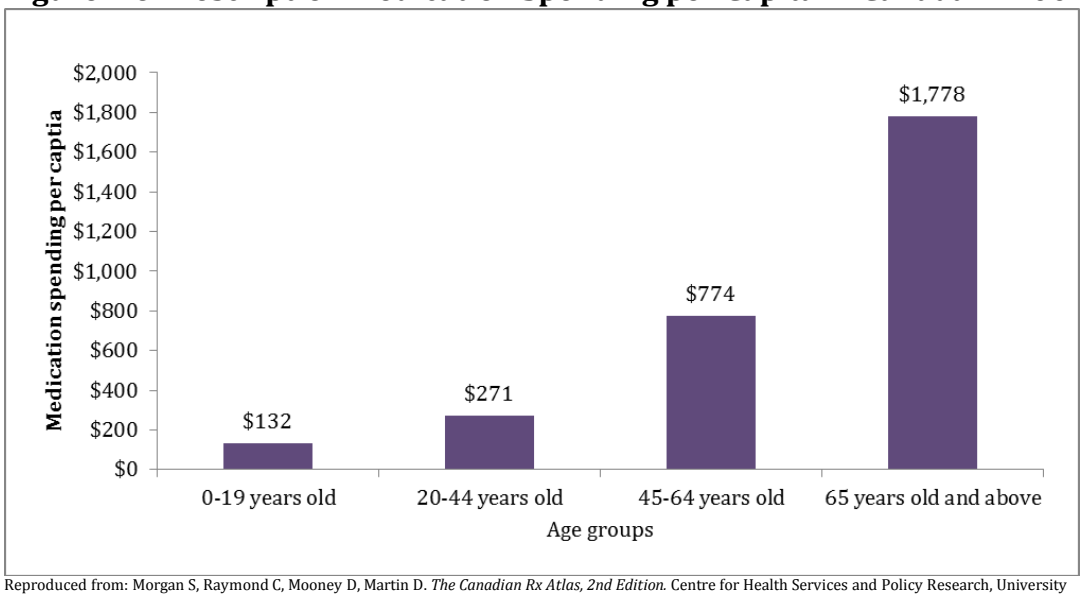
In 2009, Canadian seniors used 3.7 times more hospital services, 1.9 times more outpatient services, and 50% more emergency services compared to adults aged 20 to 64 years.(14) As a result, government health expenditures for seniors reached $11,196 per capita in 2009, which was 4.5 times higher than that for younger adults aged 20 to 64.(14) Medication use accounts for an important part of health spending on seniors. Between 2002 and 2008, more than 50% of total Canadian prescription drug costs were spent on seniors. Seniors aged 65 and older represented 13% of the total Canadian population in 2007 but consumed 41% of the drug spending in that year.(2) Furthermore, a relatively small number of medication classes account for a disproportionate amount of total medication spending among seniors. For example, almost 25% of total government spending on Canadian seniors was for two types of medications: blood-pressure-lowering agents (14.5%) and blood-cholesterol-lowering agents (10%).(2) Clearly, the ageing population is a predominant driver for medication spending (Figure 2.5) and chronic medications play a major role.(2)

**Figure 2.5 Percentage of Canadian Population (inner ring) versus Percentage of Total Prescription Medication Spending (outer ring) in 2007.**




Reproduced from: Morgan S, Raymond C, Mooney D, Martin D. *The Canadian Rx Atlas, 2nd Edition.* Centre for Health Services and Policy Research, University of British Columbia, 2008, Vancouver, B.C.(2)

**Figure 2.6 Prescription Medication Spending per Capita in Canada in 2007.**




Reproduced from: Morgan S, Raymond C, Mooney D, Martin D. *The Canadian Rx Atlas, 2nd Edition.* Centre for Health Services and Policy Research, University of British Columbia, 2008, Vancouver, B.C.(2)

The highly prevalent use of prescription medications and their associated costs are of great concern in Canada. Costs of medication use are rising so quickly it is unclear whether the current system will be sustainable over the long term.(15–19) However, prescription medications have important health benefits as well as economic benefits if used properly. Specifically, widely used medications for high blood pressure, high cholesterol, diabetes, and depression confer important protection against the negative health and economic outcomes of these devastating conditions. In fact, regular use of these agents (i.e., optimal adherence) has been associated with significant reductions in costly hospitalizations and life-threatening events as outlined below.

Medications for high blood pressure, high cholesterol, diabetes, and depression have the potential to lower morbidity, mortality, and other negative outcomes. Studies have found that first-line blood-pressure-lowering regimens and statins (i.e., blood-cholesterol-lowering medications) can reduce the risk for coronary heart disease events by 16-20%,(20,21) stroke by 17-42%,(20,22) total cardiovascular events by 11-30%,(20,21) and death by 11-17%.(20,21) Type 2 diabetes patients treated with metformin (i.e., a blood-glucose-lowering agent) were 24% less likely to die compared to those receiving placebo.(23) Further, a ten-year follow up study of metformin use was associated with a 33% lower risk of myocardial infarction and 30% lower risk of any diabetes-related death.(24) For patients with major depressive disorders (MDD), a handful of randomized control trials (RCTs) and meta-analyses have demonstrated that maintenance medication is

effective in preventing recurrence of symptoms with effects lasting from 6 months through 5 years.(25,26) Moreover, depressive disorders are often associated with high levels of non-healthcare costs because of impairment in patients' occupational functioning.(25) Antidepressants can help boost patients' work productivity by improving the work score of the Sheehan Disability Scale (SDS-work score), by which impairment of mental diseases to patients' lives is measured.(27–29) A Systematic review by Lam and colleagues found that antidepressants are associated with an improvement in the SDS-work score of 1.8-4.3 points above the placebo baseline scores in depressed patients.(30)

## 2.2 Medication Adherence

Although medications are considered an important strategy to manage the negative health and economic consequences of chronic diseases, medication non-adherence remains a major barrier to the realization of their benefits. In the 1970s, the adherence issue was first described as "compliance with therapeutic regimens" by Sackett and Haynes.(31,32) However, the term "compliance" was criticized because it implies lack of patient engagement.(31,33) In 1997, the Royal Pharmaceutical Society in UK changed its terminology from "compliance" to "concordance" in order to emphasize the importance of patients' participation in treatment, and to put the patient at the center of the decision making process.(31,33–35) More recently, the term "adherence" is widely applied to represent the interaction among patient, health care provider, and the surrounding environment including the social economic status and the health care system. The terminology of adherence assumes that patients make their best decision based on their best knowledge, motivation, skills, and resources. In 2003, adherence was defined by the World Health Organization (WHO) as: "The extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider."(4)

Good adherence is critical in achieving treatment goals among patients with chronic diseases. Patients taking more than 80% of their prescribed blood-pressure-lowering regimen were 2.3 times more likely to achieve target blood pressure levels

compared to those taking less than 80%.(36) Similarly, patients achieving 80% adherence with statin treatment for six months were associated with a 25-27% reduction of LDL-cholesterol level compared to those taking medication for fewer than 80% of the expected treatment days.(37)

Adherence is also associated with better disease outcomes and lower health-care costs. Patients exhibiting optimal adherence to blood-pressure-lowering medications can reduce risk of coronary artery disease events by 10% compared to those with lower adherence.(38) The risk of developing cerebrovascular events are 7-42% lower among individuals adherent to blood-pressure-lowering agents and 26% lower among those adherent to statins.(38,39) These health benefits of optimal adherence also result in decreased health care costs due to the avoidance of hospitalizations.(38) For example, studies indicate that diabetic patients exhibiting poor adherence to oral blood-glucose-lowering medications are 58% more likely to be hospitalized, and 81% more like to die.(40)

Unfortunately, optimal adherence is not commonly achieved in health care settings. Manifestations of non-adherence include failure to initiate the medication,(41,42) missing doses during treatment,(43) and discontinuation.(40,44–48) Pooled analyses suggest that only 54% of patients achieve optimal adherence (≥80%) for blood-cholesterol-lowering, and 59% to blood-pressure-lowering medications.(3) Further, 25-36% of Type-II diabetic patients are not adherent to oral blood-glucose-lowering medications,(49–51) and

up to 43% may discontinue oral blood-glucose-lowering medications within 3-90 days after initiation of treatment.(52) The overall cost of non-adherence has been estimated to exceed $100 billion in the United States every year;(53) thus, possible solutions to this problem are considered essential to improving the efficiency of health-care systems around the world.

### *Measures of Medication Adherence*

Medication adherence can be measured either directly or indirectly.(53,54) As illustrated in table 2.2, direct measures involve biochemical tests of the medication/metabolite in body fluids, or direct observation of administration.(53) Although the direct methods might be more accurate, they can be costly, invasive, or difficult to conduct. Besides, biochemical testing is not readily available for all medications or the test result may vary due to individual metabolism or pharmacokinetic characteristics. Thus, direct measures have little practical application for the majority of chronic medications.(54)

Indirect methods can be further stratified into subjective ratings/surveys and objective records on medication administration behaviors.(4) Subjective records include patient diaries or self-reported survey methods such as the Morisky scale,(55) which can be vulnerable to recall bias or social stigma.(31,56) Alternatively, objective measures such as pill counting and electronic monitoring

devices(4,53,54) can overestimate adherence levels(57) and often lack important information such as timing and dosage of administration.(31,56) Although information on timing of administration can be overcome using the Medication Event Monitoring System (MEMS®), it is costly and difficult to implement in large populations.(58)

Among all available measures, electronic pharmacy databases (automated pharmacy databases) are recognized as one of the most important sources of information for medication adherence research.(59,60) These databases are often developed by insurance companies or governments to record transactions, and are therefore frequently audited and validated.(60) Consequently, automated pharmacy databases contain the most standardized, accurate and cost-effective primary data on dispensation details such as date, pharmaceutical specifications, and cost.(60,61) Also, many of these databases are population-based, allowing for analyses to be carried out without exclusion of specific groups, such as vulnerable populations or individuals with specific conditions.(61) These databases usually store data for decades, allowing longitudinal studies for trends and temporal relationships between historical events (i.e., as a policy changes for copayment). Finally, electronic pharmacy databases can often be linked to health services data such as medical outpatient services, hospitalization records, or vital statistics.(59–63)

## Table 2.2 Measures of Medication Adherence.

| Categories | Sub-categories | Examples | Advantages | Disadvantages |
|---|---|---|---|---|
| Direct measures(31,56) | Biochemical measurements(31) | - Blood or urine test of medicine, metabolite, or non-toxic biological markers(31) | - Objective evidence to suggest in-take of the treatment agents(31)<br>- Probably more accurate than the indirect methods(31) | - Not available for all medications(31)<br>- Confounded by other factors such as food, absorption(31)<br>- Can be invasive(31)<br>- Variation due to individual metabolism or pharmacokinetic characteristics of the regimes(31)<br>- Difficult to perform and costly(31)<br>- Limited application for single-dose, intermittent treatment in hospital(31) |
| Indirect measures(31,56) | Subjective ratings and surveys(4) | - Self-reported rating of adherence behaviors, patient diaries(4) | - Low cost(4) | - Inaccurate ratings due to recall bias or social stigma(4) |
| | | - Standardized surveys or interviews(4) | - Information on disease-related specific behaviors may suggest prognosis of adherence(4) | - In general failing to act as reliable predictors(4) |
| | Objective records on medication administration behaviors(4,64) | - Pill counts(4) | - Easy to conduct<br>- Validated and frequently applied in randomized, controlled trials(4) | - Inaccuracy in counting leading to over-estimation of adherence(4)<br>- Lack of information on timing and dosage patterns(4)<br>- Patient didn't necessarily consume the medication(4) |
| | | - Electronic monitoring devices(4) | - Providing/suggesting medication time and dosage(4)<br>- Enhancing adherence to medicine(4) | - Costly(4)<br>- Limited usage(4)<br>- Patient didn't necessarily(4)consume the medication(4) |
| | | - Electronic pharmacy databases on patient fills and refills of the prescriptions (4,64) | - Frequently audited and validated<br>- Comparatively standardized, accurate and cost-effective primary data<br>- Allowing longitudinal studies for trends and temporal relationships<br>- Capability to link to other databases for extended analysis(64) | - Usually lack of hospital medication & OTC medication records(64)<br>- Not representing actual in-take of the drugs dispensed(64) |

### *The Impact of Cost on Medication Adherence*

A great deal of research has been conducted to identify the main drivers of medication non-adherence in order to determine the best targets for intervention. Possible causes/contributors to non-adherence have been categorized (Table 2.3) by the World Health Organization.(4) Although many of these factors likely contribute to the overall burden of non-adherence, several studies have suggested that out-of-pocket (OOP) payments (i.e., cost) are an important cause of non-adherence.(65–69)

OOP cost has been identified as a barrier to the use of preventive or life-sustaining medications such as blood-pressure-lowering regimens or statins,(66,67,69–74) resulting in poor disease control and unfavorable clinical outcomes.(66,71–74) In fact, attempts by governments or private health insurance companies to save money by reducing medication benefits (i.e., increasing OOP costs) may actually increase overall spending through higher physician visits, emergency department visits, and hospitalizations due to non-adherence.(66,70,71,73)

## Table 2.3 Factors Impacting Medication Adherence.

| Categories | Factors with positive impact | Factors with negative impact |
|---|---|---|
| Social and economic-related(4,53,75) | • Support from patient's family members or social networks(4,76,77) | • Individual's demographic factors such as age(78) female,(79,80) African or Asian American in US,(81)cultural fear or distrust of therapy(4,76)<br>• Low income and unemployment status(4,76,80,82–89)<br>• Exposure to high risk environmental circumstances(90–95) |
| Health care team/health system-related(4,53,75,96) | • The relationship between patient and the health care providers(80,82,97–100)<br>• Interaction, support, and follow up from the health care providers(98–106)<br>• Training of the health care providers, knowledge and quality of implementation of the treatment guidelines.(4,82,107,108)<br>• Performance evaluation system, incentive setting, or resources for health care(4,82)<br>• Establishment of the patient education or support system(4)<br>• Accessibility to healthcare facilities(4,76,109,110)<br>• Availability of medication supply(4,82–89,109,110) | • High treatment cost, including high medication cost(77,82–89,101,103,109–114)<br>• Patient's high out of pocket payment(4,79,109,110,115,116) |
| Condition-related(4,75,96) | • Experience of life-threatening events such as heart attack,(48) or interventional procedures(117)<br>• Patients' understanding of the disease and its symptoms, their knowledge of who to seek help from in case of emergency(112,118,119) | • Co-morbidity(118,120,121)<br>• Distressed emotions including depression(118,122–127)<br>• Duration of the disease(77) |
| Therapy-related(4,53,75) | • Clear instructions on management of disease(99,100,128)<br>• Experience with previous therapy(4,129) | • Complexity of the treatment(82–89,130–132) including frequency of changes in medications,(4,109,110) number of pharmaceuticals involved in the administration,(133–136)and frequency of dose per day.(130,137)<br>• Complexity presented as requirements for life style changes such as low salt/liquid/lipid diet, quitting of smoking and alcohol, physical activities, self-administration of medications in injectable forms(77,102,114,138,139)<br>• Duration of treatment(82–89,132)<br>• Intolerability of the medication, including adverse effects(4,82–89,132,140,141) |
| Patient-related(4,53,75,96) | • Personality traits, positive self-esteem, self-efficacy; individual beliefs, attitudes, perceptions and expectations (102,139,142–148)<br>• Active participation in disease monitoring and management (149,150) | • Concurrent addictive conditions such as alcohol abuse(151)<br>• Forgetting to take medication(125)<br>• Lack of education, health illiteracy, inadequate knowledge and skill in disease management, unaware of treatment cost and benefits, unaware of risks related to the disease, non-acceptance of monitoring, decision to omit the medication administration, or putting pharmacotherapy to low priority(4,76,82,83,113,119,125,152) |

OOP costs may be an important barrier to non-adherence; thus, cost-reduction plans are often implemented by private insurers and governments to help improve medication adherence among their beneficiaries. Most of the cost-sharing strategies can be grouped into two categories: direct and indirect, as shown in table 2.4.(65) The most frequently applied cost sharing methods include cap, coinsurance, ceilings, fixed copayment, and tier copayment.(70,71)

**Table 2.4 Cost-sharing Strategies Employed by Drug Insurance Providers**

| Categories of cost-sharing strategies | Methods of cost-sharing |
|---|---|
| Direct cost sharing(65,70,71) | **Cap**:<br>*A pre-specified number of prescriptions or medications that are free of charge*<br>**Fixed copayment**:<br>*A fixed amount per prescription paid by the patient*<br>**Tier copayment**:<br>*Fixed copayments according to whether the drug is generic or branded*<br>**Coinsurance:**<br>*A fixed percentage of the prescription's price paid by the patient*<br>**Ceilings**:<br>*The full cost paid by the patient until a pre-specified value has been reached, after which drugs are reimbursed*<br>**Maximum lifetime benefit**:<br>*Limited amount that a patient get reimbursed in his/her lifetime*<br>**Balance billing**:<br>*The additional fee exceeding the limit of reimbursement*<br>**Bonus options**:<br>*Rewards for using a certain care* |
| Indirect cost sharing(65,70,71) | **Coverage exclusions**:<br>*Medications excluded from a health plan coverage*<br>**Utilization review**:<br>*Review by the payer to adjust the reimbursement policies*<br>**Pharmaceutical-specific benefit designs**:<br>*Plans with more complex design to adjust patients' out of pocket payment (Such as a drug plan, value based insurance design (VBID), drug formulary, etc.)* |

Value Based Insurance Designs (VBID) are a method of direct cost sharing that selectively reduce patients' OOP payment for specific medications with particular health benefits or provide cost reduction opportunities customized by individual

beneficiary's disease or health profile.(153,154) VBID is commonly designed to reduce cap, fixed/tier copayment, or coinsurance. Choudhry et al examined the influence of eliminating OOP costs for clopidogrel (an anti-platelet agent) and statins (i.e. blood-cholesterol-lowering drugs) using a robust prospective randomized design,(155) in which increased adherence levels were observed among individuals randomized to free medications, despite that the absolute differences in 12 month adherence rates were relatively small (i.e., +4% for clopidogrel and +2.8% for statins).(68,155) Other studies have also reported association between decreased OOP costs and mediation adherence; however, the reported effect sizes varied considerably.(156–160)

Higher adherence can result in better disease control, fewer complications, reduced utilization of medical services, and eventual reductions in overall health care costs.(154,161) Chernew et al reported that reduced copayments increased adherence by 7-14%(162) while Choudhry and colleagues found adherence increases of 4-6% when cardiac medications were provided free of charge.(68) In Choudhry's study, significant reductions in total major vascular events or revascularizations was found among subjects receiving free medications in a follow-up period of three years.(68) In other studies, OOP saving was found associated with higher likelihood of medication adherence, reducing spending on non-pharmaceutical medical services.(163–167) These studies suggest that investing in medication costs can be cost-neutral for health care providers as a result of reduced need for downstream health services to treat major health outcomes.(68)

***The Saskatchewan Seniors' Drug Plan (SDP)***

On July 1st, 2007, the government of Saskatchewan implemented the Seniors' Drug Plan (SDP) in order to improve access to essential medication use for chronic diseases among residents aged 65 or older. All beneficiaries of the SDP were automatically enrolled on their 65th birthday(168) to receive all covered medications for a maximum of $15 per prescription. On July 1st, 2008, the plan was restricted to those who had applied, and were eligible for the federal age credit of $75,480 based on the annual net income reported on Line 236 of individual's previous year income tax form.(168,169)

In the fiscal year of 2007 to 2008 (April 1st, 2007 to March 31st, 2008), 76,057 individuals were covered and nearly 50% of the government expenditures on prescription medications for seniors (i.e., $67 million) was spent on the Seniors' Drug Plan.(170) In 2010, spending on the SDP increased to $107 million (66% of Saskatchewan government expenditures on medications for seniors).(171) However, to date no study has rigorously examined the impact of the SDP in terms of medication utilization and adherence.

The objectives of this study were: 1) to examine trends in the utilization of medications in Saskatchewan prior to, and following the implementation/modification of the SDP; and 2) to estimate the impact of the SDP on medication non-adherence for major chronic conditions in Saskatchewan.

# Chapter 3 Methods

## 3.1 Data Sources

The Saskatchewan Ministry of Health maintains major databases containing health service information including the Person Registry System (PRS), Prescription Drug Plan (PDP) database, Hospital Discharge Abstract Database (DAD), and Medical Services Branch (MSB) database. These health services databases can be linked by the unique identification number derived from each individual's encrypted health services number.(60,172)

The PDP database captures all outpatient prescriptions covered by the provincial drug formulary. Over 90% of the Saskatchewan population is registered beneficiaries; the remaining 9% are individuals who receive drug benefits from the federal government (e.g., First Nations or Canadian Armed Forces). A record is generated for each prescription dispensed to beneficiaries containing the following information: a unique patient identification number, Drug Identification Number (DIN), medication name, dispensation date, quantity dispensed, prescriber's identification number (encrypted), total cost, and payment by government. PDP does not capture information for prescriptions excluded from the provincial list of covered medications, physician provided samples, over-the-counter (OTC) drugs, or medications used during hospitalization.(60)

Data for beneficiaries' outpatient medical services are collected in the databases of Medical Services Branch, including Physician Services Claims Files containing patient information (e.g., age, sex, location of residence) and diagnostic/service information (e.g., 3-digit ICD-9 code, service code, billing information), and Physician Files including physician information (e.g., physician's gender, and specialty). During 2002-2003, 74% of all outpatient services were claimed by physicians under a fee-for-service model, while 26% were from non-fee-for-service physicians.(60) Physician claim data in Saskatchewan go through a process of systematic computerized validity checks; accuracy and potential errors are continuously monitored electronically, with manual reviews in case of suspicion on data accuracy.(60,172)

In-hospital information is collected in the Hospital Discharge Abstract Database, with standardized disease coding based on ICD-9 (up until March 31st, 2001), or ICD-10-CA (since April 1st, 2001).(172–174) Since 2001, each hospital discharge record can record up to 25 diagnoses (172,175) and up to 20 procedures.(172,176) In addition, information on date of admission, type of hospital, duration of stay, and date of discharge are also captured. The hospital services database, however, does not capture information of emergency room visits.(64) Overall, Saskatchewan health-administrative databases have been used frequently in health services research and appear to provide valid information on diagnoses and drug use.(60,177–180)

For this study, health-administrative data from Saskatchewan was abstracted and electronically linked with encrypted identification numbers at the individual subject level. These datasets are currently available to the Saskatchewan Health Quality Council (HQC) via a secure virtual private network connection to a data warehouse located in eHealth Saskatchewan's servers. HQC's access to and use of these data are regulated by a data sharing agreement (DSA) between the Ministry of Health and HQC. The DSA stipulates which data fields HQC can access in each database, expectations for protection of patient privacy in the use and storage of data, as well as in any reporting based on the data. As per HQC policy, only selected HQC staff (i.e., the project manager, researchers, and programmer/analysts for this project) have access to these datasets. Data extracted from the data warehouse was maintained in folders within the eHealth data warehouse or on HQC's secure network that is not connected to the internet and is located within HQC's secure data area. Data back-up from the secure server to tape is performed within the secure area and the back-up media remain in the secure area. The secure data area is a physical space within HQC that has restricted access. All individual-record level data, whether in electronic or hard copy format, remains in the secure data area.

## 3.2 Objective 1

**Examine province-wide trends in the utilization of medications prior to, and following the implementation/modification of the SDP.**

***Hypothesis***

Increased medication utilization will be observed in the period after implementation of the SDP on July 1st, 2007, compared with the period before.

***Sub-objective 1-A***

***Describe trends in overall medication utilization between 2005 and 2009.***

To accomplish this objective, an interrupted time-series analysis of medication utilization was conducted using the prescription drug database between July 1st, 2005 and June 30th, 2009. This observation period includes two years (2005-2007) before implementation of the SDP and two years following (2008-2009). Medication utilization was measured by calendar month. Subjects were eligible for inclusion in any interval if they were 65 years of age or older on the first day of the given month. To account for temporal changes in drug utilization,

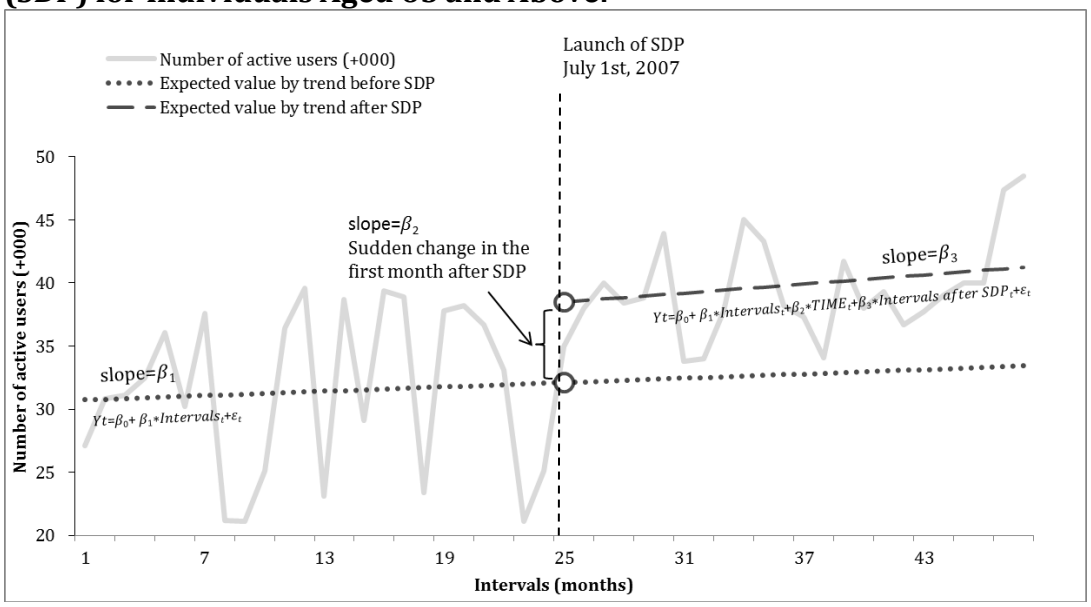
individuals between 40-64 years, who did not receive the SDP benefit, were included as a control group.

In each interval, four indicators of overall drug use were calculated: a) the total number of active users (i.e., individuals with at least one dispensation in each interval); b) total number of dispensations in each interval; c) inflation adjusted total cost of all dispensations in each interval; and d) inflation adjusted total government share of medications dispensed in each interval. All indicators were expressed as continuous values and age and sex standardized to the January 2007 covered population to eliminate the potential impact of changing demographics over time. The method of direct standardization followed the procedure described by Merlo.(181) For instance, to calculate the standardized active users, the number of beneficiaries registered in the PRS in January 2007 was selected as the standard population. Within the standard population, we divided the individuals according to their age into groups of 40-64, 65-69, 70-74, 75-79, and ≥ 80, and further stratified by sex within each age-category to get the total number of beneficiaries within each stratum. Next, active user rates in each interval were calculated within these same strata using interval-specific number of active users as numerator and interval-specific number of beneficiaries as denominator. The rates were then multiplied by the corresponding number of active beneficiaries in the January 2007 covered population, to obtain the standardized numbers of active users.

### *Data Analysis*

A time series analysis was performed to test the impact of the SDP on each age and sex-standardized measure of drug utilization.(182,183) Segmented regression models were constructed in the following groups: a) patients 65 years of age and older (i.e., patients eligible for SDP benefits starting July 1, 2007), patients between 40 and 64 years of age (i.e., patients not eligible for the SDP on July 1, 2007), and all patients combined (i.e., patients aged 40 and older). For example, to test the impact of the SDP on total number of active users among seniors, the following model (Equation 3.1) was built (Figure 3.1):

**Figure 3.1 Hypothetical Trends in the Number of Active Drug Plan Beneficiaries before versus after Implementation of the Seniors' Drug Plan (SDP) for Individuals Aged 65 and Above.**




$Y_t = \beta_0 + \beta_1 * Intervals_t + \beta_2 * TIME_t + \beta_3 * Intervals\ after\ SDP_t + \varepsilon_t$ (Equation 3.1)

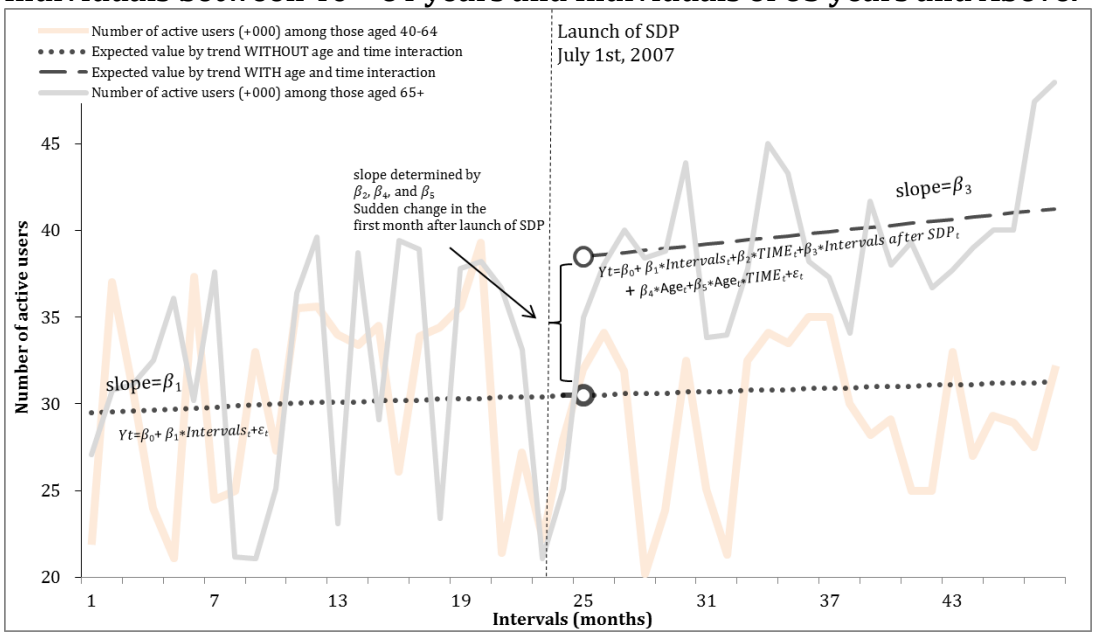
Whereas: $Y_t$ is the number of active users at a particular interval. $Intervals_t$ are defined as the number of months since the beginning of the observation period (e.g., the interval of July-2005 =1, August-2005 = 2, …, June-2009 = 48); $TIME_t$ is the status of the SDP coverage of that particular interval (i.e., the intervals before July-2007 = 0, while the intervals after July-2007 =1); $Intervals\ after\ SDP_t$ is the number of months since the launch of the SDP (e.g., the intervals before July-2007 =0, the interval of July-2007 =1, August-2007 = 2, …, June-2009 = 24). The $\beta$-coefficients estimate: the level of change of the outcome before the SDP (i.e., $\beta_1$ = baseline growth in utilization), the level of change of the outcome immediately following the launch of the SDP (i.e., $\beta_2$ = change in outcome after the SDP implementation), and the change in the rate of growth of the outcome after the SDP implementation (i.e., $\beta_3$ = change in growth rate above baseline); $\varepsilon_t$ represents the error not explained by the model at interval t. Further, tests of autocorrelation of Durbin-Watson Statistics(182) were performed. Terms to correct autocorrelation were introduced into the model if significant autocorrelation was detected. Akaike Information Criterion (AIC) and total R-square were obtained to indicate the fitness of the model. Similar approaches for applying segmented regression models in medication utilization analyses has been reported by others.(184,185)

These drug utilization trends were also examined in a model containing all individuals without stratification by age (Figure 3.2). Analysis of the full cohort allowed for a parallel assessment of the impact by SDP in order to control for the

influence of temporal trends that may have confounded the before-after analysis. However, for the model including both comparator groups (i.e., those <65 versus ≥65), the impact of the SDP was assessed using an interaction term between Age and TIME ($Age_t * TIME_t$, Equation 3.2). Specifically, the effect of 'TIME' (i.e., 0=before and 1=after) would be dependent on the level of age (i.e., 0= less than 65; 1= 65 and older), because neither age-group was exposed to the SDP before July 1, 2007 while only those 65 and older were exposed to the SDP following this date.

$$Y_t = \beta_0 + \beta_1 * Intervals_t + \beta_2 * TIME_t + \beta_3 * Intervals\ after\ SDP_t + \beta_4 * Age_t + \beta_5 * Age_t * TIME_t + \varepsilon_t \quad \text{(Equation 3.2)}$$

**Figure 3.2 Hypothetical Trends in the Number of Active Beneficiaries before versus after Implementation of the Seniors' Drug Plan (SDP) for Individuals between 40 – 64 years and Individuals of 65 years and Above.**




Utilization results were also stratified by general pharmacological categories outlined by the American Hospital Formulary Service (AHFS, Table 3.1), as well as the use of potential inappropriate medications (PIMs) based on the 2003 Beers

Criteria.(186) Beers criteria are widely applied internationally for the identification of PIM use among the elderly population at or above 65 years (Table 3.2).(187,188)

**Table 3.1 Planned Stratification of the Drug Utilization Analysis Based on the Pharmacologic-Therapeutic Classification System of the American Hospital Formulary Service (AHFS).**

| AHFS Code | Class of Medications |
|---|---|
| 8:00 | Anti-infective Agents |
| 12:00 | Autonomic Drugs |
| 20:00 | Blood Formation, Coagulation, and Thrombosis Agents |
| 24:00 | Cardiovascular Drugs |
| 28:00 | Central Nervous System Agents |
| 40:00 | Electrolytic, Caloric, and Water Balance |
| 48:00 | Respiratory Tract Agents |
| 52:00 | Eye, Ear, Nose, and Throat (EENT) Preparations |
| 56:00 | Gastrointestinal Drugs |
| 68:00 | Hormones and Synthetic Substitutes |
| 84:00 | Skin and Mucous Membrane Agents |
| 86:00 | Smooth Muscle Relaxants |
| 88:00 | Vitamin |

Saskatchewan Health. *Drug Plan Formulary V62, 2013.* Regina, SK.(189)

**Table 3.2 Classifications of Potentially Inappropriate Medications among Seniors Aged 65 and Above.**

| AHFS Code | Class of Medications |
|---|---|
| 28:08.04 | Cyclooxygenase-2 (COX-2) Inhibitors, Other Nonsteroidal Anti-inflammatory agents |
| 28:08.08 | Opiate Agonists |
| 28:08.12 | Opiate Partial Agonists |
| 28:12.04 | Barbiturate (as Anticonvulsant) |
| 28:12.08 | Benzodiazepine |
| 28:16.04 | Tricyclics and Other Norepinephrine reuptake Inhibitor, Antidepressant |
| 28:16.08 | Atypical Antipsychotic, Phenothiazine, Thioxanthene |
| 28:24.08 | Benzodiazepine |
| 28:24.92 | Anxiolytic, Sedative, and Hypnotic |

Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med.* 2003 Dec 8-22;163(22):2716-24.(186)

***Sub-objective 1-B***

***Examine trends in medication utilization for specific chronic disease medications***

Trends in utilization were also examined for specific medications commonly used to manage highly prevalent chronic conditions in Saskatchewan. The chronic medications included blood-cholesterol-lowering, blood-pressure lowering, blood-glucose-lowering, and antidepressant agents (Table 3.3). Utilization was described by total dispensations and total number of distinct users. In addition, the number of individuals receiving each medication was further stratified into incident users and prevalent users. Incident users were defined as those eligible active users with at least one dispensation for a chronic medication during a specific interval but no dispensations within the specific medication class in the previous 365 days. In contrast, prevalent users were defined as those with a history of previous dispensations for the specific class of medications in the prior 365 days. To ensure that all individuals can be classified consistently, individuals were excluded from this sub-analysis if they were not continuously covered by the Saskatchewan drug plan for the minimum of 365 days prior to the starting of the study interval.

**Table 3.3 Specific Chronic Medication Classes Tracked Before versus After the Implementation of the Seniors' Drug Plan (SDP) in Saskatchewan.**

| Therapeutic Category | Generic Names | AHFS Code |
|---|---|---|
| Blood-cholesterol-lowering medications | HMG-CoA reductase inhibitor (i.e., statin) | ➢ 24:06 |
| Blood-pressure-lowering medications | ➢ All blood-pressure-lowering Agents | ➢ 24:08 |
| Oral blood-glucose-lowering medications, and insulin | ➢ All blood-glucose-lowering including insulin | ➢ 68:20 |
| Antidepressant agents | ➢ Serotonin-Norepinephrine Reuptake Inhibitor (SNRI)<br>➢ Selective Serotonin Reuptake Inhibitor (SSRI) | ➢ 28:16.04 |

American Society of Health-System Pharmacists (ASHP). *AHFS Drug Information ® 2008.*(190)

## 3.3 Objective 2

**Estimate the impact of the SDP on medication adherence for selected chronic conditions in Saskatchewan.**

### *Hypothesis*

The SDP will not significantly improve adherence to chronic medications in Saskatchewan.

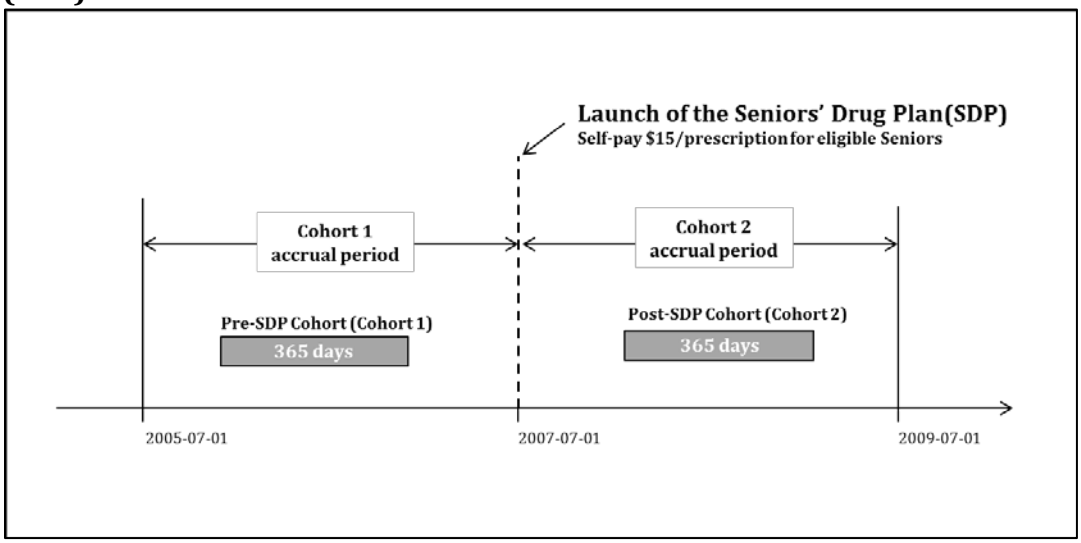
### *Study design*

A retrospective cohort study examining 1-year adherence to selected chronic medications (blood-pressure-lowering agents, blood-cholesterol-lowering medications, oral blood-glucose-lowering drugs, or anti-depressants) before and after implementation of the SDP (i.e., using historical controls). Previous studies have clearly demonstrated that adherence levels decline much faster among incident users;(40,45) therefore, separate analyses were carried out for incident and prevalent users of chronic medications.

### *Subjects*

Two distinct 'recruitment periods' were used to identify eligible subjects in each comparator group, as shown in Figure 3.3. For the historical control group (i.e., those receiving medications before the SDP), subjects were included if they began receiving chronic medications (Table 3.4) between July 1st, 2005 and June 30th, 2006 (i.e., 1 to 2 years before the SDP launch). The exposure group included individuals who had received an eligible medication between July 1st, 2007 and June 30th, 2008 (i.e., after the SDP). The earliest dispensation during each accrual period was considered the index date (i.e., the beginning of observation). Eligible subjects were at least 40 years old on the index date, and continuously registered beneficiaries for Saskatchewan health services during the observation period. Patients between 40 and 64 years were included as a parallel control group because they did not receive the SDP benefit after July 1, 2007.

**Figure 3.3 Selection of Cohorts for the Comparison of Adherence in the "Pre" versus "Post" Periods following Implementation of the Seniors' Drug Plan (SDP).**




Both cohorts were stratified by prior use of the target medication. Incident users were defined by no dispensations within the same therapeutic category during 365 days prior to the index date. Therefore, adherence in these individuals was examined during their first year of treatment when the highest risk for non-adherence occurs. In contrast, prevalent users were defined as users receiving dispensations within 365 days preceding the index date. In this way, the incident use and prevalent use cohorts remained mutually exclusive. In order to properly define the user type, the incident users were required to have at least 365 days of continuous registration under Saskatchewan health services prior to the index date, while prevalent users were required to be covered for at least 1,825 days prior to the index date, so as to determine their years on the study medications.

Adherence was examined for four major chronic medications in Saskatchewan (blood-cholesterol-lowering, blood-pressure-lowering, blood-glucose-lowering, and antidepressant agents). For subjects receiving more than one of the eligible medication classes (e.g., receiving a blood-cholesterol-lowering agent and a blood-pressure lowering agent simultaneously), pharmacy claims of each class was followed up as a separate observation. The target classes of the medications are identified in Table 3.4.

Following July 1st, 2007 beneficiaries of the SDP paid a maximum cost of $15 for each prescription. Therefore, patients receiving medications costing ≤ $15 were not impacted by the SDP. As such, we performed a stratified analysis according to medication cost. Patients were categorized into the group "≤ $15" if they had received at least one dispensation of the study medication (table 3.4) costing ≤ $15 within the observation period. Individuals receiving medications >$15 were also examined in subgroup analyses categorized as those who had received at least one dispensation of the study medication costing ">$30", otherwise "$16-30".

Some individuals were receiving benefits from other programs such as social assistance, resulting in a reduction of OOP costs (i.e., total medication cost minus the drug plan payment) to less than $15 per dispensation. We thereby conducted another stratified analysis to examine the impact of the SDP with or without these "other benefits". Subjects were categorized as receiving another benefit program if

they had at least one dispensation for a study medication where the OOP was reduced below $15 during the observation period.

**Table 3.4 Chronic Medications Included in an Evaluation of Adherence Before versus After the Implementation of the Seniors' Drug Plan (SDP) in Saskatchewan.**

| Therapeutic Category | Classification of interested medications |
|---|---|
| Blood-cholesterol-lowering medications | ➢ HMG-CoA reductase inhibitor or "statin" |
| Blood-pressure lowering medications | ➢ Angiotensin-Converting-Enzyme Inhibitor (ACEI) or Angiotensin Receptor Blockers (ARB)<br>➢ Dihydropyridine Calcium Channel Blocker (DHP CCB) |
| Oral blood-glucose-lowering medications | ➢ Metformin (a type of biguanide)<br>➢ Glyburide (a type of sulfonylurea) |
| Antidepressant agents | ➢ Selective Serotonin Reuptake Inhibitor (SSRI)<br>➢ Serotonin-Norepinephrine Reuptake Inhibitor (SNRI) |

American Society of Health-System Pharmacists (ASHP). *AHFS Drug Information ® 2008.*(190)

### *Adherence Outcome Measures*

Medication adherence was estimated using the Medication Possession Ratio (MPR).(191) In order to calculate this measure, the days-supplied from each dispensation was estimated individually for each specific medication using previously accepted approaches. For statin, ACE inhibitors/Angiotensin receptor blocker (ACEI/ARB) and antidepressant, number of days supplied for each dispensation was fixed at 34 days corresponding to the typical refill duration by Saskatchewan pharmacies.(189) The approach has been used previously to assess medication adherence with good consistency with other measures.(191) For the oral blood-glucose-lowering agents (metformin, and glyburide), the number of days

supplied was defined according to the quantity dispensed because the maintenance drug schedule of the Saskatchewan drug plan formulary allows up to 100-day supplies to be dispensed for these agents.(192) Specifically, for dispensations with a quantity ≤ 34, the number of days supplied was equal to the quantity (1:1 ratio). For quantities between 35 and 68, the number of days supplied was equal to the quantity dispensed divided by two. For quantities from 69 to 132, the quantity was divided by three; for quantities between 133 and 136, quantity was divided by four. Dispensations with quantities higher than 136 were assumed to have 100 supply days. Extensive sensitivity testing and descriptive analyses were conducted on the specific strategies used to estimate the number of days supplied.

The MPR was calculated by identifying all dispensations for the medication of interest occurring on index date and the following 365 days. The total of all days-supplied from these dispensations was divided by 365 to obtain an adherence percentage. For patients who were hospitalized during the follow up period, the number of days staying within the hospital was subtracted from the denominator because medication use cannot be captured for inpatients.(64) A similar approach has been applied by other researchers with acceptable validity.(193)

If the number of days supplied of medication was greater than 365 days, it was truncated to 365 days. Truncation is commonly applied for prevention of false inflation of the adherence level, while not impacting the estimate of optimal adherence (i.e., MPR ≥80%).(194,195) Adherence <120% was assumed to result

from the accumulation of doses from early refills while adherence ≥ 120% was manually investigated to identify possible misclassification due to erroneous estimation of the days supplied variable. Individuals who switch between medications of the same medication class were considered continuous users.

***Data Analysis***

Logistic regression models were constructed to test the impact of the SDP on the endpoint of optimal adherence (i.e., MPR ≥ 80%) at one year. This definition is the most frequently applied criteria in medication adherence studies.(36,196,197) To quantify the impact of the SDP, an interaction term was created between TIME (i.e., before/after the SDP) and Age Category (i.e., <65/≥65) because only those ≥65 were exposed to the SDP in the 'after period' whereas the SDP was not available in the 'before' period. The null hypothesis asserted that the impact of TIME (before vs after) is not impacted by one's age, whereas the alternative hypothesis is that the impact of TIME would depend on a person's age because only those ≥65 were eligible to receive the SDP. The odds ratios (OR) and 95% confidence intervals for the impact of the SDP were determined from the equation $e^{\beta}$ where $\beta$ represents the coefficient for the interaction term.

In order to minimize the effect of confounding factors between patients in the before versus after cohorts, several additional variables were included in the regression model. A theoretical framework of adherence determinants (Table 2.3)

have been proposed by the WHO(4) and grouped in the following categories: social and demographic factors, health system-related factors, condition related factors, and therapy related factors.(178,198–202) Variables from each category were captured and introduced into the model as confounding covariates (Table 3.5).

**Table 3.5 Variables Included in Regression Models to Control for Confounding in the Evaluation of Adherence Before versus After the Implementation of the Seniors' Drug Plan (SDP) in Saskatchewan.**

| Category | Variables | Variable categories |
|---|---|---|
| Social and demographic factors | • Age at index date(78) | • 0 for age 40-46, 1 for age 65-59, 2 for 70-74, 3 for 75-79, 4 for age 80 and above |
| | • Sex(79,80) | • 0 for males, 1 for females |
| | • Inflation adjusted income level quintile imputed from residential neighborhood(76,80,84,85) | • Quintiles of 5 levels |
| | • Rural/Urban residence(203) | • 0=rural, 1=urban |
| Health system-related factors | • Specialty of the prescriber based on index dispensation date(204–207) | • 0=family physician, 1= Specialist |
| | • Receipt of other health plan benefit | • 0=no dispensations with OOP < $15 in observation period, otherwise =1 |
| | • Number of physician visits with 'prescriber' during observation year(98,104) | • Quintiles of 5 levels |
| | • Number of distinct physicians providing service during observation year besides prescriber(80,97) | • Quintiles of 5 levels |
| Condition-related factors | • Charlson Comorbidity Index (CCI) Score(175,208–210) | • Quintiles of 5 levels |
| | • Presence of a target chronic diseases*(118,120,121) | • 0 = not diseased, 1=diseased |
| | • Number of nights spent in hospital during observation year(48,77,117) | • zero nights in hospital=0, one or more nights in hospital = 1 |
| | • Previous hospitalization of at least one day for any reason within 3 months prior to the index date(48,117) | • 0 for no hospitalizations, 1 for at least one hospitalization<br>• |
| Therapy-related factors | • The specific target medication initiated(68) | • 1 for statin, 2 for ACEI/ARB, 3 for CCB, 4 for metformin, 5 for glyburide, 6 for SSRI, 7 for SNRI. |
| | • Number of dispensations of the target medication in previous year (*for prevalent users only)*(191) | • Quintiles of 5 levels |
| | • Pill burden. Number of distinct medications received within the first 3 months of the observation period by AHFS class(211,212) | • Quintiles of 5 levels |
| | • Dispensation cost | • 1=receiving at least one dispensation of studied medication with total cost <$15 during the observation period, otherwise=0 |
| | • Prevalentuser | • 1=receiving at least one dispensation of studied medication within 365 days prior to the initial date of observation, otherwise=0 |

*Target chronic diseases: Hypertensive disease (ICD9:401-405 ;ICD10CA: I10-I13, I15), Coronary Heart Disease (ICD9:410-414 ;ICD10CA: I20-I25), Stroke(ICD9:430-438 ;ICD10CA: I60-69), Diabetes Mellitus(ICD9:250 ;ICD10CA: E10-E14), Hyperlipidemia(272 ;ICD10CA: E78), Depression(ICD9:311 ;F32). Cases were identified by at least two outpatients or one hospital diagnosis occurring during a two year period starting one-year before the index dispensation.(213–215)

Prior to building the multivariable models, descriptive tests were performed with each explanatory variable to determine if transformations (quadratic or categorical) provide more clinically and statistically relevant associations with the dependent variable. However, all of the variables listed in Table 3.5 were retained in the multivariable model to minimize the risk of confounding on the assessment of adherence between the cohorts. Values of Quasi-Akaike Information Criterion (QIC) were obtained from models with and without confounders to test the model fitness.

Generalized linear models with generalized estimating equations (GEE) were used to account for the dependence between outcome measurements from the same patient (i.e., patients may have received $\geqslant$1 target medications).(216,217) The models were developed using an exchangeable working correlation structure, which assumes a constant correlation between all pairs of measurements.(218–220) For non-linear situations, the generalized linear model with GEEs produces estimates that describe the population-average effect rather than a subject-specific effect of the SDP, which is produced using a random-effects model.(221) In this research, the population-average approach will produce estimates that are relevant to the payer (i.e. the government), who is primarily interested in the impact of the SDP at the population level.

Subgroup analyses were conducted based on type of medication, sex, age, hospitalization (0 vs ≥ 1 hospitalized days during the observation period), and

medication cost (<$15 and ≥$15) using the same modelling approach described above. In addition, several sensitivity analyses were carried out on the estimation of MPR. Specifically, the number of days supplied for each dispensation was estimated using alternative methods to determine if the specific approach impacted the results. For example, statins are most commonly prescribed as one tablet/capsule per day; thus, the number of days supplied of each statin dispensation was estimated by using the quantity dispensed and also by the fixed estimate of 34 days per each dispensation.(222) However, the risk for bias originating from any of the MPR calculations was felt to be low because the approach was consistently applied to all patients (i.e., control patients and SDP recipients) in each model. SAS statistic software, version 9.3, (SAS Institute Inc., Cary, NC, USA) was used to conduct all analyses.(223)

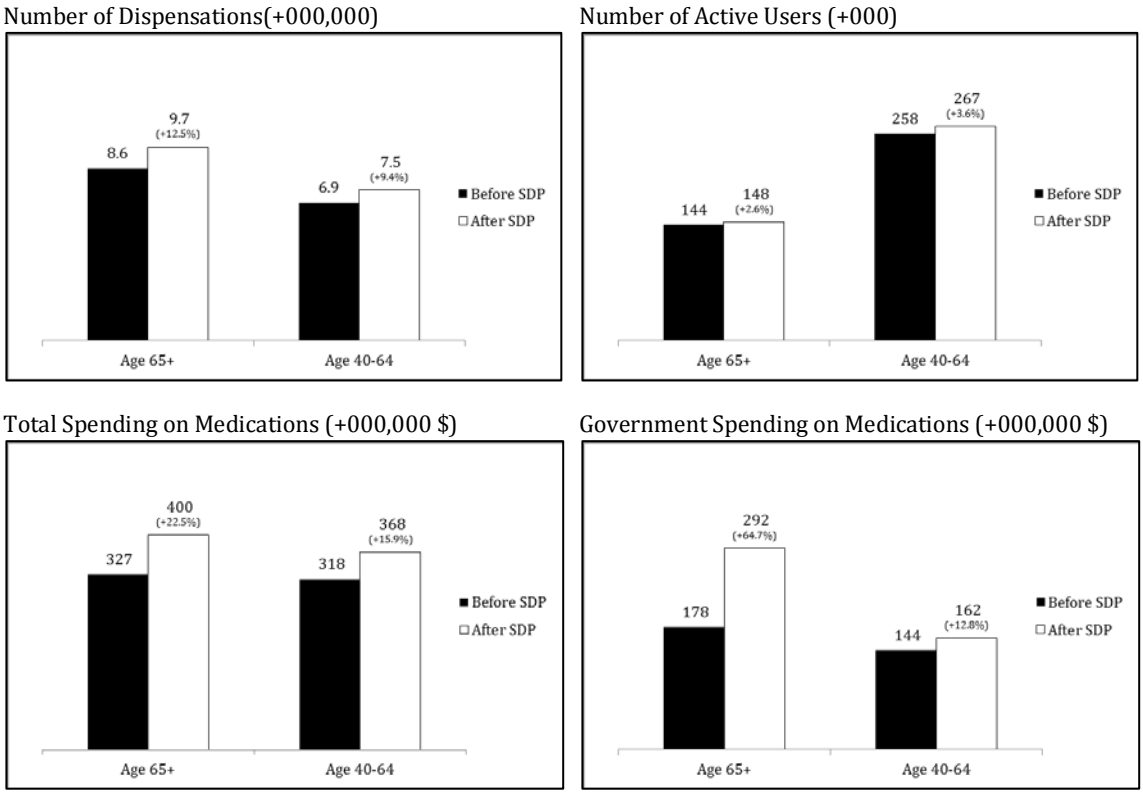
# Chapter 4 Results

## 4.1 Impact of the SDP on Medication Unitization Trend Change in Saskatchewan

### *Impact of the SDP on Medication Utilization and Cost*

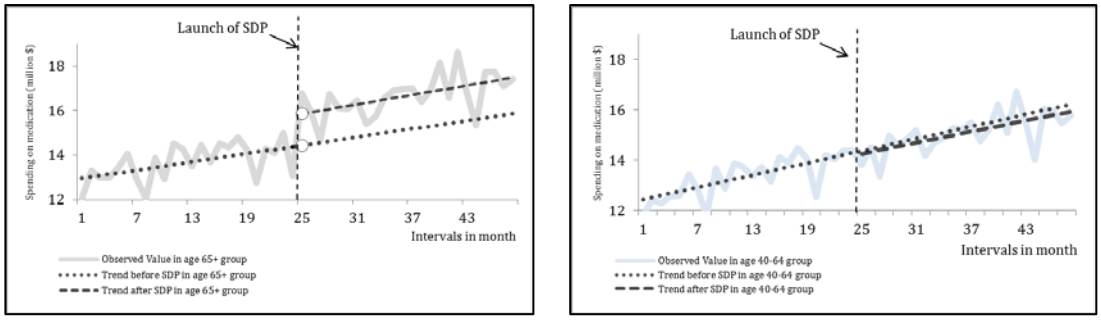
Between July 1st 2005 and June 30th, 2009, the number of individuals receiving at least one prescription medication dispensation in Saskatchewan grew steadily from 344,963 in the first 12 months to 361,041 in the last 12 months. Growth was observed in both seniors (i.e., ≥65 years of age) and adults between 40 and 64 comparing two years before and after the SDP launch; the number of seniors using medications increased by 2.6% while numerically higher growth (3.6%) was observed in the younger adult group not receiving the SDP. However, seniors exhibited higher increases in medication spending (i.e., both total and government share) and the total number of dispensed medications following the SDP implementation (Figure 4.1).

**Figure 4.1 Medication Utilization and Costs Based on the Two-years Before Implementation of the Seniors' Drug Plan (SDP) and Two-years Following (i.e., July 1st, 2005 to Jun 30th, 2009).**




Time series analyses, stratified by age, show a clear increase in monthly medication spending on seniors following the SDP implementation. In contrast, no temporal increase was observed among individuals aged 40 to 64; thus, it would appear that no external factors were causing increases in drug use at the time of the SDP implementation (Figure 4.2).

**Figure 4.2 Standardized Monthly Medication Spending (in millions) in Saskatchewan among Seniors (left) and Adults 40-64 years (right) before and after Implementation of the Seniors' Drug Plan.**




When the drug utilization analysis was restricted to seniors (≥65 years old), estimates for the increase in total medication spending following the launch of the SDP was 9.8% (95% CI: 3.7-16.0%) or approximately $1.4 million per month, while government spending increased by 45.9% (95% CI: 40.0-52.0%) for an increase of $3.7 million per month. The total number of dispensations increased by 6.0% (95% CI: 3.1%-9.0%), and the number of active users increased by 3.9% (95% CI: 2.1-5.8%) reflecting absolute monthly increases of 22,261 and 3,799 respectively. Among individuals 40 to 64 years of age, no significant differences between the pre and post period were observed for any of the drug utilization endpoints (Figure 4.3 to 4.5).

**Figure 4.3 Standardized Monthly Government Spending on Medications (in millions) in Saskatchewan among Seniors (left) and Adults 40-64 years (right) before and after Implementation of the Seniors' Drug Plan.**

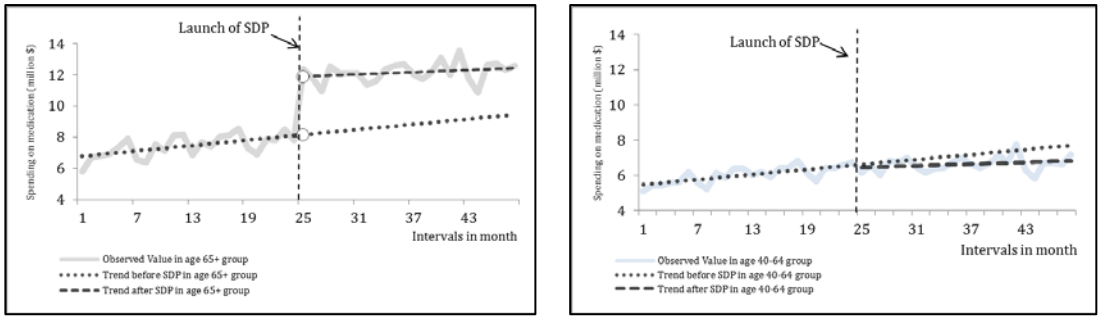



**Figure 4.4 Standardized Monthly Number of Dispensations (+000) in Saskatchewan among Seniors (left) and Adults 40-64 years (right) before and after Implementation of the Seniors' Drug Plan.**

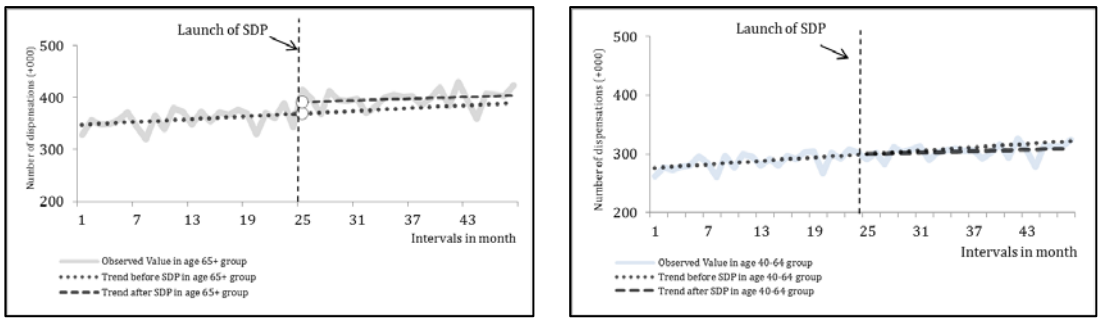
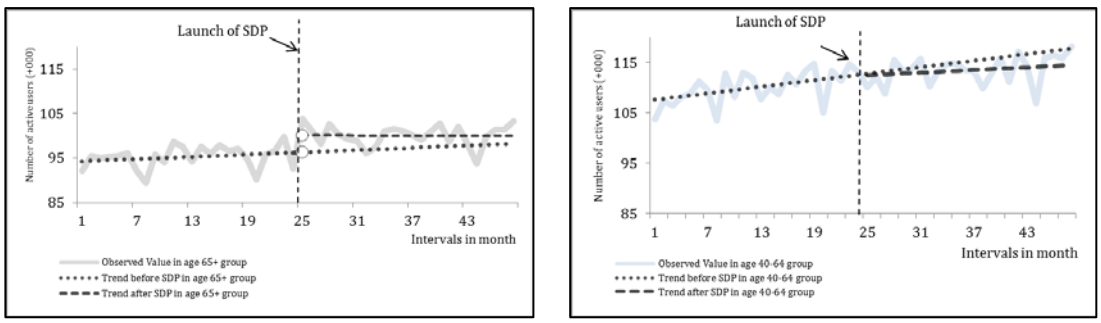



**Figure 4.5 Standardized Monthly Number of Active Users (+000) in Saskatchewan among Seniors (left) and Adults 40-64 years (right) before and after Implementation of the Seniors' Drug Plan.**



When these drug utilization endpoints were examined in a model containing all individuals ≥40 years (i.e., not just those ≥65), the overall impact attributed to the SDP was slightly attenuated. Total dispensations increased by 5.8% (95% CI: 3.8% to 7.8%), total number of active users increased by 2.2% (95% CI: 0.4% to 3.9%), total cost increased 7.8% (95% CI: 5.0% to 10.6%), and total government share increased by 47.5% (95% CI: 42.8% to 52.2%). However, the rate of growth of medication utilization (i.e., the slope following the SDP implementation) did not increase compared to the previous periods. In fact, the growth rate of government spending was lower compared with the period preceding the SDP implementation. Upon Durbin-Watson test, autocorrelation was found positive (DW=1.5346). Improvement of fitness was observed in the model with autocorrelation-correction terms (AIC=2,089, Total R-Square=0.94) comparing with the models without (AIC=2,118, Total R-Square=0.91).

***Medication Utilization Change within General Pharmacologic Categories and Specific Medication Classes***

Statistically significant increases in the number of dispensations were observed for 10 out of the 12 pre-defined AHFS-pharmacologic categories. Cardiovascular agents (AHFS 024) were associated with the highest absolute increase in total number of dispensations at 8,873 per month (+6.2%; 95% CI: 2.0% to 10.3%), while the highest relative increases were observed with autonomic drugs

(AHFS 012) and gastrointestinal drugs (AHFS 056) at 18.8% (95% CI: 13.7% to 23.9%), and 16.9% (95% CI: 13.0% to 20.9%) respectively. Use of potentially inappropriate medications also increased by 3.9% (95% CI: 1.1% to 6.7%) Analysis of number of active users suggest similar finding. In contrast, utilization of hormones and synthetic substitutes (AHFS 068) and vitamins (AHFS 088) was not statistically different in the period following the SDP implementation (Table 4.1).

**Table 4.1 Change in Standardized Monthly Number of Dispensations after Implementation of the Seniors' Drug Plan (SDP) among Saskatchewan Seniors.**

| Medication classes | Monthly Change of Number of Dispensations | Change in percentage | 95% CI |
|---|---|---|---|
| Autonomics | 1,733 | 18.8% | 13.7% to 23.9% |
| Gastrointestinal drugs | 3,559 | 16.9% | 13.0% to 20.9% |
| Eye, Ear, Nose, and Throat (EENT) preparations | 848 | 8.1% | 5.4% to 10.8% |
| Antibiotics | 743 | 6.7% | 2.5% to 10.9% |
| Cardiovascular agents | 8,873 | 6.2% | 2.0% to 10.3% |
| Blood formation, coagulation, and Thrombosis agents | 865 | 6.0% | 3.4% to 8.5% |
| Skin and mucous membrane agents | 328 | 5.9% | 2.5% to 9.3% |
| Selected Chronic Medications | 6,599 | 5.4% | 1.2% to 9.6% |
| Central nervous system agents | 2,616 | 5.0% | 2.1% to 8.0% |
| Smooth muscle relaxants | 122 | 4.8% | 1.1% to 8.5% |
| Potential Inappropriate Medications (PIM) | 1,847 | 3.9% | 1.1% to 6.7% |
| Electrolytic, caloric, and water balance | 997 | 3.2% | 0.1% to 6.3% |
| Hormones and synthetic substitutes | 832 | 2.5% | -1.6% to 6.6% |
| Vitamins | 55 | 1.4% | -2.4% to 5.1% |

### *Medication Utilization Change within Specific Chronic Disease Medications*

Of the four major classes of chronic medications analyzed, blood-cholesterol-lowering agents (i.e., statins) had the highest increase in monthly number of dispensations at 8.5% (95% CI: 3.4% to 13.5%), followed by the blood-pressure-lowering medications at 6.2% (95% CI: 2.0% to 10.5%), and the antidepressant agents at 3.6% (95% CI: 1.3% to 5.9%). In contrast, utilization of blood-glucose–lowering agents (i.e., diabetes medications) did not change significantly, either in number of dispensations (-0.5%, 95% CI: -6.2% to 5.2%) or in active users (0.4%, 95% CI: -3.8% to 4.6%). These results are summarized in Table 4.2 and 4.3. Metformin and glyburide accounted for 60% of the medications used in the glucose-lowering class. This observation is important because almost half of the dispensations for these medications cost $15 or less before the SDP implementation; thus, a high number of dispensations in this category were not impacted by the SDP benefit (Figure 4.6).

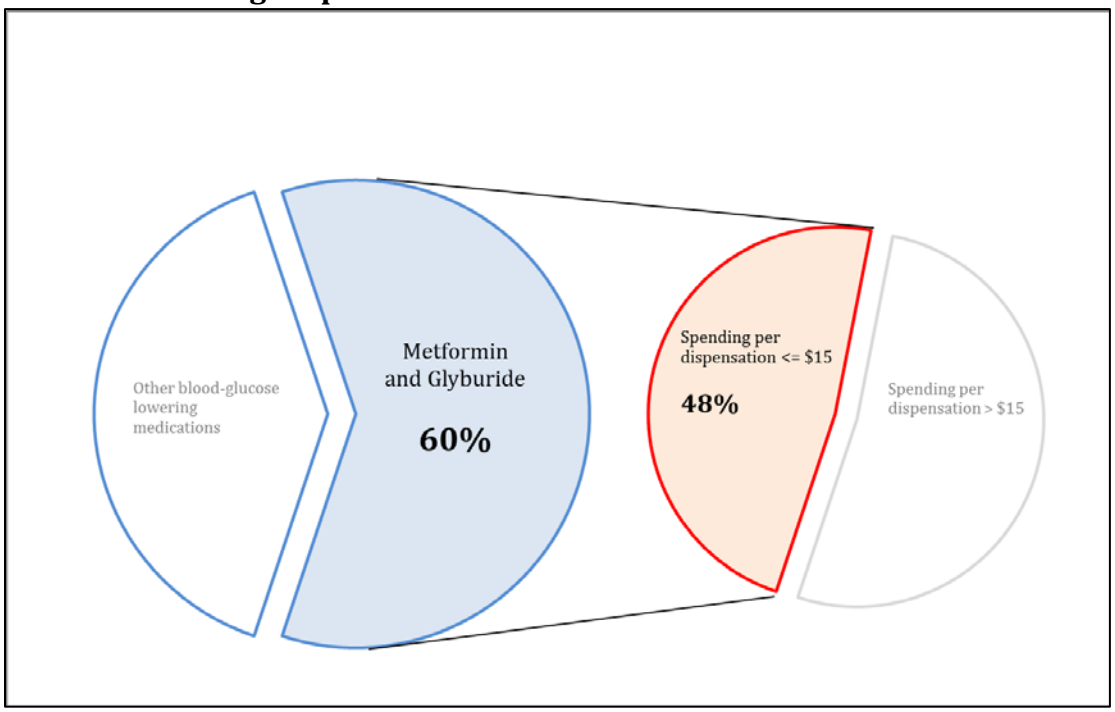
**Table 4.2 Change in Standardized Monthly Number of Dispensations among Seniors after Implementation of the Seniors' Drug Plan (SDP) in Saskatchewan.**

| Type of Medication | Monthly Change of Number of Dispensations | Change in percentage | 95% CI |
|---|---|---|---|
| Blood-cholesterol-lowering agents | 2,428 | 8.5% | 3.4% to 13.5% |
| Blood-pressure-lowering agents | 3,743 | 6.2% | 2.0% to 10.5% |
| Antidepressant agents | 569 | 3.6% | 1.3% to 5.9% |
| Blood-glucose-lowering agents | -82 | -0.5% | -6.2% to 5.2% |

**Table 4.3 Change in Standardized Monthly Number of Dispensation after Implementation of the Seniors' Drug Plan (SDP) among senior residents in Saskatchewan.**

| Type of Medication | Monthly Change of Number of Dispensations | Change in percentage | 95% CI |
|---|---|---|---|
| Blood-cholesterol-lowering agents | 1,795 | 7.0% | 3.0% to 10.9% |
| Blood-pressure-lowering agents | 2,479 | 5.0% | 1.8% to 8.2% |
| Antidepressant agents | 444 | 3.4% | 1.3% to 5.5% |
| Blood-glucose-lowering agents | 46 | 0.4% | -3.8% to 4.6% |

**Figure 4.6 Frequency of Metformin and Glyburide as a Percentage of All Glucose-Lowering Dispensations in Saskatchewan.**




The impact of the SDP was not consistent for utilization among incident versus prevalent users of these major chronic medication classes. Among prevalent users, overall monthly dispensation counts increased by 5.4% (95% CI: 1.3% to 9.5%) following implementation of the SDP. Increases were clearly observed for

prevalent users of blood-cholesterol-lowering, blood-pressure lowering, and antidepressant agents but not blood-glucose-lowering medications (Table 4.4). In contrast, among individuals classified as incident users, no significant difference was observed in dispensations for these specific classes overall. Further, no differences were observed for three out of the four individual medication classes. Only blood-cholesterol-lowering agents were associated with greater use following the SDP implementation (Table 4.5).

**Table 4.4 Change in Standardized Monthly Number of Dispensations after Implementation of the Seniors' Drug Plan (SDP) versus before the SDP among Prevalent Users.**

| Type of Medication | Monthly Change of Number of Dispensations for Prevalent Users | Change in percentage | 95% CI |
|---|---|---|---|
| Blood-cholesterol-lowering agents | 2,383 | 8.5% | 3.6% to 13.4% |
| Blood-pressure-lowering agents | 3,640 | 6.1% | 1.9% to 10.3% |
| Antidepressant agents | 554 | 3.7% | 1.3% to 6.1% |
| Blood-glucose-lowering agents | -43 | -0.3% | -6.0% to 5.5% |
| All 4 classes of chronic medications | 6,464 | 5.4% | 1.3% to 9.5% |

**Table 4.5 Change in Standardized Monthly Number of Dispensations after Implementation of the Seniors' Drug Plan (SDP) versus before the SDP among Incident Users.**

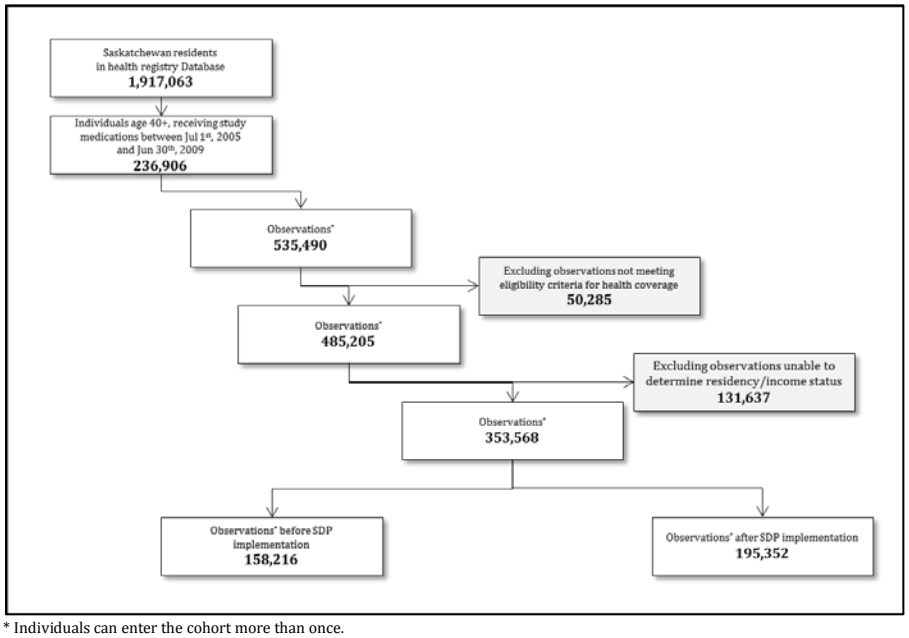
| Type of Medication | Monthly Change of Number of Dispensations for Incident Users | Change in percentage | 95% CI |
|---|---|---|---|
| Blood-cholesterol-lowering agents | 101 | 16.9% | 8.0% to 25.8% |
| Blood-pressure-lowering agents | 19 | 3.1% | -9.5% to 15.7% |
| Antidepressant agents | -6 | -1.1% | -10.2% to 8.1% |
| Blood-glucose-lowering agents | -30 | -14.4% | -35.8% to 7.0% |
| All 4 classes of chronic medications | 26 | 1.3% | -8.0% to 10.7% |

## 4.2 Estimate the Impact of the SDP on Medication Adherence for Selected Chronic Disease Medications in Saskatchewan.

### *Characteristics of the Study Population*

Among 1.9 million individuals registered in the provincial health care database, 236,906 received at least one dispensation for an eligible chronic medication between July 2005 and June 2009 for a total of 535,490 observations. We further excluded 50,285 adherence observations because of insufficient follow-up and 131,637 with incomplete residency or income information (Figure 4.7). The number of observations in stratified analysis is reported in Appendix A.

**Figure 4.7 Patient Flow Diagram for the Retrospective Cohort Study Examining the Impact of the Seniors' Drug Plan (SDP) in Saskatchewan on Medication Adherence.**




* Individuals can enter the cohort more than once.

Overall, 353,568 observations were retained for the primary analysis of adherence. The study population was made up of two 'seniors' cohorts: the pre-SDP group (i.e., control group) consisting of 62,759 observations, and the post-SDP group (i.e., exposure group) consisting of 83,950 observations. Also, two additional control groups were identified among adults aged 40-64 years (pre- and post-SDP). Baseline differences between individuals in the pre-SDP period versus the post-SDP period frequently reached statistical significance; however, few of the differences were considered clinically important (Table 4.6). The cohort of seniors was of advanced age (73.3±5.9 in pre-SDP cohort, and 74.0±6.3 in post-SDP cohort), 56.3% females, and 64.6% living in urban areas. Hypertension was the most prevalent diagnosis among this population (71.7%), followed by diabetes (37.8%). The majority of seniors (83.4%) were prevalent users of the medication being studied and 95.0% of medications were prescribed by family physicians. ACEI and ARB (43.8%) were the most frequently received medications in this group, followed by statins (31.1%). On average, patients received five different medications within the first three months of observation.

Individuals aged 40-64 had fewer visits to physicians, fewer medications, and lower Charlson scores compared to the senior cohorts. Use of antidepressant agents was more frequent while blood-cholesterol-lowering, blood-pressure-lowering, and oral blood-glucose-lowering agents were used by a lower percentage of patients compared to the seniors (Table 4.6).

**Table 4.6 Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP).**

| | | Age 65+ | | Age 40-64 | |
|---|---|---|---|---|---|
| | | Pre-SDP N=62,759 | Post-SDP N=83,950 | Pre-SDP N=95,457 | Post-SDP N=111,402 |
| **Gender** | | | | | |
| | Females | 35,786 (57.0%) | 46,752 (55.7%) | 47,508 (49.8%) | 54,454 (48.9%) |
| **Age at index date** | | 73.3±5.9 | 74.0±6.3 | 53.5±6.6 | 53.9±6.5 |
| | 40-64 | | | 95,457 (100%) | 111,402 (100%) |
| | 65-69 | 19,786 (31.5%) | 24,644 (29.4%) | N/A | N/A |
| | 70-74 | 18,219 (29.0%) | 22,538 (26.8%) | N/A | N/A |
| | 75-79 | 14,667 (23.4%) | 19,359 (23.1%) | N/A | N/A |
| | ≥80 | 10,087 (16.1%) | 17,389 (20.7%) | N/A | N/A |
| **Residency type** | | | | | |
| | Urban | 40,214 (64.1%) | 54,592 (65.0%) | 64,322 (67.4%) | 75,606 (67.9%) |
| | Rural | 22,545 (35.9%) | 29,358 (35.0%) | 31,135 (32.6%) | 35,796 (32.1%) |

*Pre-SDP = observation period before the launch of the SDP on Jul 1st, 2007; Post-SDP = observation period after the launch of the SDP

**Table 4.6(continued) Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP).**

| | Age 65+ | | Age 40-64 | |
|---|---|---|---|---|
| | Pre-SDP | Post-SDP | Pre-SDP | Post-SDP |
| | N=62,759 | N=83,950 | N=95,457 | N=111,402 |
| **Prescriber type** | | | | |
| Family Physician | 59,435 (94.7%) | 79,919 (95.2%) | 90,528 (94.8%) | 106,490 (95.6%) |
| Specialist | 3,324 (5.3%) | 4,031 (4.8%) | 4,929 (5.2%) | 4,912 (4.4%) |
| **Hyperlipidemia** | | | | |
| | 13,816 (22.0%) | 17,736 (21.1%) | 24,131 (25.3%) | 27,551 (24.7%) |
| **Hypertension** | | | | |
| | 46,051 (73.4%) | 59,145 (70.5%) | 54,266 (56.9%) | 61,774 (55.5%) |
| **Coronary Heart Disease (CHD)** | | | | |
| | 15,918 (25.4%) | 21,684 (25.8%) | 16,733 (17.5%) | 19,891 (17.9%) |
| **Stroke** | | | | |
| | 5,302 (8.5%) | 8,808 (10.5%) | 8,585 (9.0%) | 11,567 (10.4%) |
| **Diabetes** | | | | |
| | 22,539 (35.9%) | 32,921 (39.2%) | 34,327 (36.0%) | 42,549 (38.2%) |
| **Depression** | | | | |
| | 5,821 (9.3%) | 7,988 (9.5%) | 21,273 (22.3%) | 24,046 (21.6%) |
| **Medication class** | | | | |
| Statin | 18,877 (30.1%) | 26,772 (31.9%) | 25,022 (26.2%) | 31,284 (28.1%) |
| ACEI/ARB* | 28,120 (44.8%) | 36,113 (43.0%) | 34,228 (35.9%) | 39,326 (35.3%) |
| CCB* | 734 (1.2%) | 814 (1.0%) | 459 (0.5%) | 429 (0.4%) |
| Metformin | 6,578 (10.8%) | 9,361 (11.2%) | 9,790 (10.3%) | 11,863 (10.7%) |
| Glyburide | 3,045 (4.9%) | 3,344 (4.0%) | 3,697 (3.9%) | 3,439 (3.1%) |
| SSRI* | 3,891 (6.2%) | 5,570 (6.6%) | 14,504 (15.2%) | 16,092 (14.4%) |
| SNRI* | 1,334 (2.1%) | 1,976 (2.4%) | 7,757 (8.1%) | 8,969 (8.1%) |
| **Type of user** | | | | |
| Incident Users | 10,626 (16.9%) | 13,748 (16.4%) | 22,320 (23.4%) | 24,178 (21.7%) |
| Prevalent Users | 52,133 (83.1%) | 70,202 (83.6%) | 73,137 (76.6%) | 87,224 (78.3%) |

*ACEI = angiotensin-converting-enzyme inhibitor; ARB= angiotensin receptor blocker; CCB=calcium channel blocker; SSRI=selective serotonin reuptake; SNRI= serotonin-norepinephrine reuptake inhibitors

**Table 4.6 (Continued) Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP).**

| | | Age 65+ | | Age 40-64 | |
|---|---|---|---|---|---|
| | | Pre-SDP | Post-SDP | Pre-SDP | Post-SDP |
| **Group** | **Category** | **N=62,759** | **N=83,950** | **N=95,457** | **N=111,402** |
| **Income Level (+000 $)** | | 24.7± 7.0 | 24.8 ± 7.0 | 25.9 ± 7.5 | 26.0 ± 7.6 |
| | Quintile 1: 3.2-19 | 13,798(22.0%) | 18,246(21.7%) | 17,467(18.3%) | 20,254(18.2%) |
| | Quintile 2: 19.1-$22 | 13,717(21.9%) | 18,145(21.6%) | 17,326(18.2%) | 19,748(17.7%) |
| | Quintile 3: $22.1-$26 | 12,902(20.6%) | 17,292(20.6%) | 18,804(19.7%) | 21,940(19.7%) |
| | Quintile 4: $26.1-$31 | 11,492(18.3%) | 15,607(18.6%) | 20,218(21.2%) | 23,866(21.4%) |
| | Quintile 5: ≥$31 | 10,850(17.3%) | 14,660(17.5%) | 21,642(22.7%) | 25,594(23.0%) |
| **Number of visits to prescribers during the observation period** | | 10.6 ± 10.5 | 11.3 ± 11.4 | 7.9 ± 8.5 | 7.9 ± 8.6 |
| | Quintile 1 : 0-3 | 11,352(18.1%) | 14,017(16.7%) | 27,713(29.0%) | 32,773(29.4%) |
| | Quintile 2 : 4-5 | 9,736(15.5%) | 12,491(14.9%) | 18,402(19.3%) | 21,725(19.5%) |
| | Quintile 3 : 6-8 | 13,294(21.2%) | 17,469(20.8%) | 20,101(21.1%) | 22,960(20.6%) |
| | Quintile 4 : 9-14 | 14,726(23.5%) | 20,079(23.9%) | 16,956(17.8%) | 19,729(17.7%) |
| | Quintile 5 : ≥15 | 13,651(21.8%) | 19,894(23.7%) | 12,285(12.9%) | 14,215(12.8%) |
| **Number of non-prescriber physicians visited during the observation period** | | 4.1 ± 3.9 | 3.9 ± 3.8 | 3.5 ± 3.6 | 3.3 ± 3.5 |
| | Quintile 1 : 0 | 7,238(11.5%) | 9,538(11.4%) | 14,481(15.2%) | 17,510(15.7%) |
| | Quintile 2 : 1-2 | 19,868(31.7%) | 27,379(32.6%) | 33,387(35.0%) | 40,310(36.2%) |
| | Quintile 3 : 3 | 8,341(13.3%) | 11,208(13.4%) | 12,280(12.9%) | 14,343(12.9%) |
| | Quintile 4 : 4-6 | 15,182(24.2%) | 20,440(24.4%) | 21,113(22.1%) | 23,924(21.5%) |
| | Quintile 5 : ≥7 | 12,130(19.3%) | 15,385(18.3%) | 14,196(14.9%) | 15,315(13.8%) |
| **Charlson Comorbidity Index (CCI) score** | | 4.1 ± 1.1 | 4.3 ± 1.4 | 2.1 ± 1.0 | 2.1 ± 1.1 |
| | Quintile 1 : 1 | 0(0.0%) | 0(0.0%) | 26,648(27.9%) | 28,302(25.4%) |
| | Quintile 2 : 2 | 0(0.0%) | 0(0.0%) | 43,460(45.5%) | 50,715(45.5%) |
| | Quintile 3 : 3 | 17,675(28.2%) | 21,723(25.9%) | 21,876(22.9%) | 27,361(24.6%) |
| | Quintile 4 : 4 | 29,929(47.7%) | 37,350(44.5%) | 1,867(2.0%) | 2,332(2.1%) |
| | Quintile 5 : ≥5 | 15,155(24.2%) | 24,877(29.6%) | 1,606(1.7%) | 2,692(2.4%) |
| **Number of nights in hospital during the observation period** | | 2.1 ± 7.0 | 2.1 ± 7.5 | 1.1 ± 5.4 | 1.1 ± 5.6 |
| | Subgroup1 : =0 | 42,255(67.3%) | 57,317(68.3%) | 74,540(78.1%) | 87,998(79.0%) |
| | Subgroup2 : >0 | 20,504(32.7%) | 26,633(31.7%) | 20,917(21.9%) | 23,404(21.0%) |
| **Number of dispensations of target medication within 365 days prior to the index date among prevalent users** | | 6.5 ± 4.4 | 6.7 ± 4.5 | 5.8 ± 4.6 | 6.0 ± 4.7 |
| | Quintile 1 : 0 | 10,626(16.9%) | 13,748(16.4%) | 22,320(23.4%) | 24,178(21.7%) |
| | Quintile 2 : 1-4 | 11,948(19.0%) | 15,742(18.8%) | 18,700(19.6%) | 21,923(19.7%) |
| | Quintile 3 : 5-8 | 11,990(19.1%) | 15,416(18.4%) | 18,855(19.8%) | 21,503(19.3%) |
| | Quintile 4 : 9-10 | 18,151(28.9%) | 25,062(29.9%) | 23,040(24.1%) | 28,523(25.6%) |
| | Quintile 5 : ≥11 | 10,044(16.0%) | 13,982(16.7%) | 12,542(13.1%) | 15,275(13.7%) |
| **Number of distinct medications received within first 3 months of the observation period** | | 4.7 ± 2.6 | 5.0 ± 2.6 | 3.8 ± 2.5 | 4.0 ± 2.5 |
| | Quintile 1 : 1-2 | 12,435(19.8%) | 13,525(16.1%) | 33,031(34.6%) | 36,302(32.6%) |
| | Quintile 2 : 3 | 10,739(17.1%) | 12,799(15.3%) | 17,854(18.7%) | 20,746(18.6%) |
| | Quintile 3 : 4 | 10,549(16.8%) | 13,861(16.5%) | 14,418(15.1%) | 17,243(15.5%) |
| | Quintile 4 : 5-6 | 15,816(25.2%) | 22,641(27.0%) | 17,621(18.5%) | 21,170(19.0%) |
| | Quintile 5 : ≥7 | 13,220(21.1%) | 21,124(25.2%) | 12,533(13.1%) | 15,941(14.3%) |
| **Number of hospitalizations 3 months prior to the index date** | | 0.2 ± 0.4 | 0.1 ± 0.4 | 0.1 ± 0.3 | 0.1 ± 0.3 |
| | Subgroup1 : =0 | 54,627(87.0%) | 73,561(87.6%) | 87,440(91.6%) | 102,628(92.1%) |
| | Subgroup2 : >0 | 8,132(13.0%) | 10,389(12.4%) | 8,017(8.4%) | 8,774(7.9%) |

The crude percentage of patients achieving optimal adherence (i.e., MPR≥80%) increased slightly among seniors following the SDP implementation (i.e., 70.8% vs 68.5%). However, the change was even smaller in the cohorts aged 40-64 (i.e., 63.6% vs 62.9%). Analysis of each independent medication revealed a trend that was consistent with the overall comparison (Table 4.7).

**Table 4.7 Percentage of Patients Achieving Optimal Adherence (MPR≥80%).**

| | Age 65+ | | Age 40-64 | |
|---|---|---|---|---|
| | **Pre-SDP** | **Post-SDP** | **Pre-SDP** | **Post-SDP** |
| **Statin** | 63.3% | 66.8% | 58.1% | 59.6% |
| **ACEI/ARB*** | 75.1% | 76.9% | 71.8% | 72.1% |
| **CCB*** | 77.7% | 76.8% | 71.9% | 73.9% |
| **Metformin** | 66.8% | 68.9% | 65.0% | 64.6% |
| **Glyburide** | 60.9% | 60.8% | 58.4% | 55.0% |
| **SSRI*** | 56.1% | 59.9% | 50.9% | 51.8% |
| **SNRI*** | 63.0% | 67.7% | 60.1% | 63.2% |
| **All classes** | **68.5%** | **70.8%** | **62.9%** | **63.6%** |

*ACEI = angiotensin-converting-enzyme inhibitor; ARB= angiotensin receptor blocker; CCB=calcium channel blocker; SSRI=selective serotonin reuptake; SNRI= serotonin-norepinephrine reuptake inhibitors

### *Impact of the SDP on Medication Adherence in the Study Population*

Evidence supporting a positive effect of the SDP was observed in the multivariable regression analysis. A significant interaction between 'TIME' (i.e., before and after the launch of the SDP) and age category (i.e., seniors aged 65 and above, or aged 40-64) was observed in the model examining the endpoint of optimal adherence at one year (i.e., MPR ≥ 80%). Seniors aged ≥65 exhibited a significantly

higher odds of adherence following the launch of the SDP (OR=1.08, 95% CI: 1.04 to 1.11, table 4.8). The value of Quasi-Akaike Information Criterion (QIC) reduced from 452,373 in the partial model to 356,929 in the full model, indicating improvement of fitness when all variables were included.

**Table 4.8 Odds of Achieving Optimal Adherence* Among Individuals Receiving the Seniors' Drug Plan (SDP) Compared to Controls (i.e., patients < 65 and patients observed before July 1, 2007).**

| | **Partial GEE model with terms:** 'AgeGroup', 'Time', 'AgeGroup*Time' | | | | **Full GEE model with terms:** 'AgeGroup', 'Time', 'AgeGroup*Time', and all available covariates | | | |
|---|---|---|---|---|---|---|---|---|
| | Estimate | Standard Error | QIC* | Odds Ratio (95% CI) | Estimate | Standard Error | QIC* | Odds Ratio (95% CI) |
| **AgeGroup*TIME** | 0.08 | 0.012 | 452,373 | 1.09 (1.06 to 1.11) | 0.074 | 0.016 | 356,929 | 1.08 (1.04 to 1.11) |

*Optimal adherence was defined as a Medication Possession Ratio ⩾ 80%; QIC=Quasi-Akaike Information Criterion.

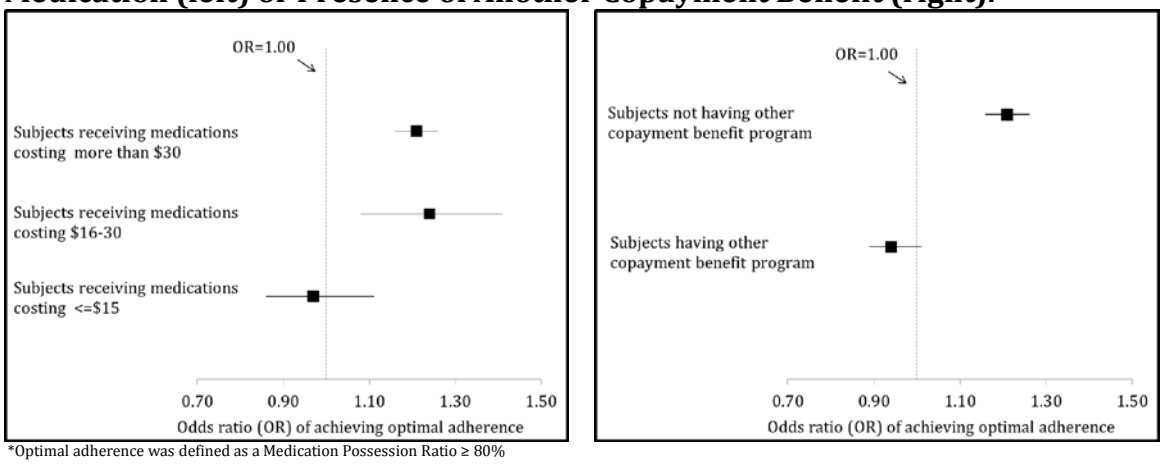
### *Stratified Analysis of Impact by the SDP on Medication Analysis for Specific Groups*

Among the subgroup of patients ≥65 years of age, the odds of achieving optimal adherence following the SDP was consistent with the primary analysis (OR=1.05, 95% CI: 1.02 to 1.07) The cohort of patients from 40 to 64 who were not eligible for the SDP did not exhibit significant difference in the odds of achieving optimal adherence in the pre- versus post-SDP period (OR=0.96, 95% CI: 0.94 to 0.98).

The effect of the SDP was consistently demonstrated in subgroups of patients receiving medications with total medication spending per dispensation between $16

and $30 (OR =1.24, 95% CI: 1.08 to 1.41) as well as those with total spending per dispensation ≥ $30 (OR = 1.21, 95% CI: 1.16 to 1.26). In contrast, the subgroup of patients receiving medications costing less than $15 experienced no benefit of the SDP (OR=0.97, 95% CI: 0.86 to 1.11). Similarly, patients receiving other benefits from the Ministry of Health (i.e., defined as those receiving at least one discounted dispensation with self-payment less than $15), the odds of optimal adherence was not increased following the launch of the SDP (OR=0.94, 95% CI: 0.89 to 1.01). To the contrary, among individuals who were not covered by another provincial medication benefit program, seniors were 21% more likely to exhibit optimal adherence following the SDP implementation (OR= 1.21, 95% CI: 1.16 to 1.26, Figure 4.8)

**Figure 4.8 Adjusted Odds Ratio of Achieving Optimal Adherence* Following Implementation of the Seniors' Drug Plan (SDP) Stratified by Retail Cost of Medication (left) or Presence of Another Copayment Benefit (right).**

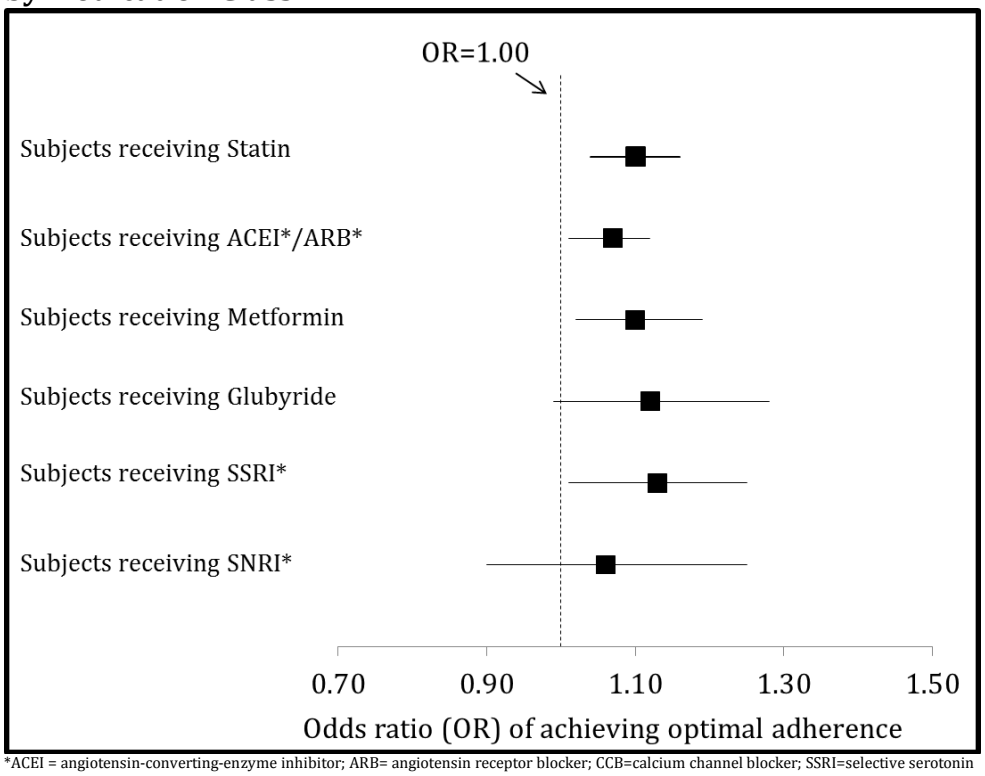



*Optimal adherence was defined as a Medication Possession Ratio ≥ 80%

When cohorts were stratified by medication class, blood-cholesterol-lowering agents (i.e., statin), blood-pressure-lowering medications (i.e., ACEI/ARB), the

blood-glucose-lowering agents Metformin, and the antidepressant SSRI were significantly impacted by the SDP (OR=1.10, 95% CI: 1.04 to 1.16 for statin; OR=1.07, 95% CI: 1.011 to 1.12 for ACE/ARB; OR=1.10, 95% CI: 1.02 to 1.19 for metformin; OR=1.13, 95% CI: 1.01 to 1.25 for SSRI). Although all OR values were higher than one, the odds of achieving optimal adherence for the rest medication classes were not significantly different compared to the cohorts un-exposed to the SDP (Figure 4.9).

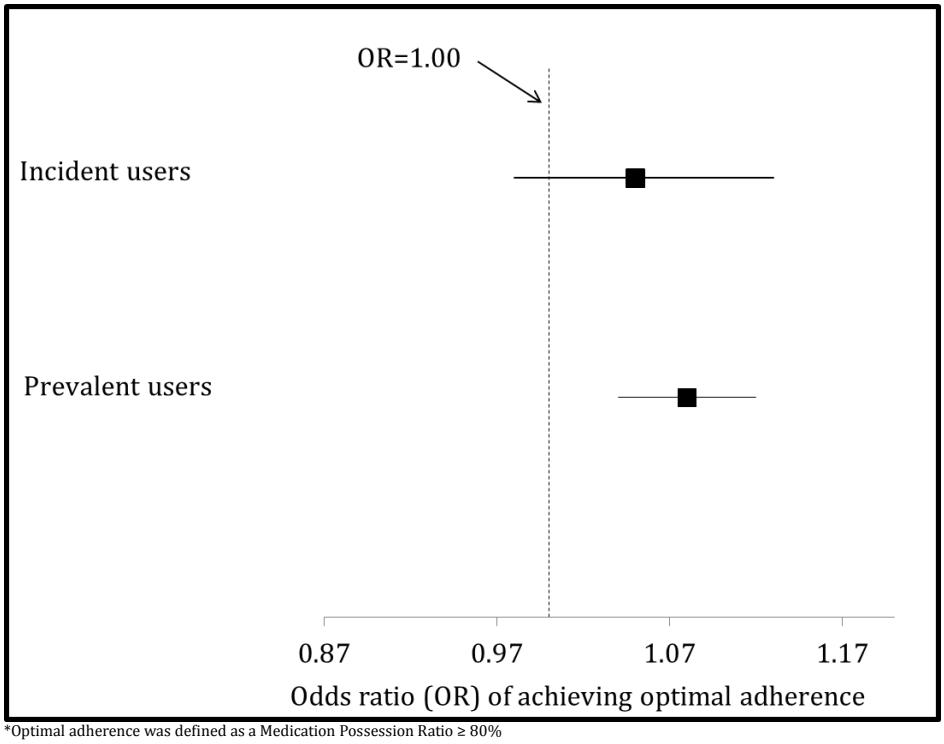
**Figure 4.9 Adjusted Odds Ratio of Achieving Optimal Adherence† Following Implementation of the Seniors' Drug Plan (SDP), Stratified by Medication Class.**




*ACEI = angiotensin-converting-enzyme inhibitor; ARB= angiotensin receptor blocker; CCB=calcium channel blocker; SSRI=selective serotonin reuptake; SNRI= serotonin-norepinephrine reuptake inhibitors
†Optimal adherence was defined as a Medication Possession Ratio ≥ 80%

The SDP was significantly associated with higher odds of achieving good adherence for prevalent users of chronic medications (OR of prevalent users = 1.08, 95% CI: 1.04 to 1.12), but not for incident users (OR of incident users=1.05, 95% CI: 0.98 to 1.13, Figure 4.10).

**Figure 4.10 Adjusted Odds Ratio of Achieving Optimal Adherence* Following Implementation of the Seniors' Drug Plan Stratified into Incident (i.e., no prior use) versus Prevalent Users of the medication.**

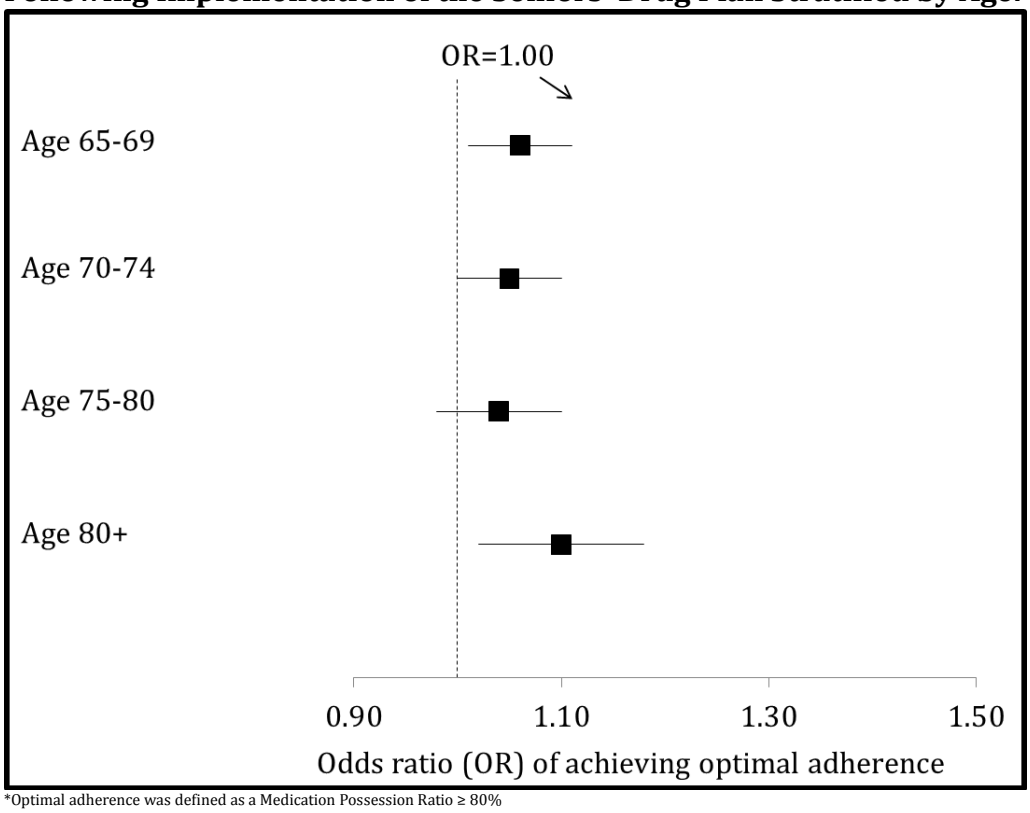



*Optimal adherence was defined as a Medication Possession Ratio ≥ 80%

Both males and females had increased odds of achieving good adherence following the launch of the SDP (OR of males=1.12, 95% CI: 1.07 to 1.18; OR of females=1.04, 95% CI: 1.00-1.09). Also, the impact of the SDP appeared relatively

consistent among subgroups of seniors based on age (i.e., 65-69, 70-75, 75-79, and over 79, Figure 4.11).

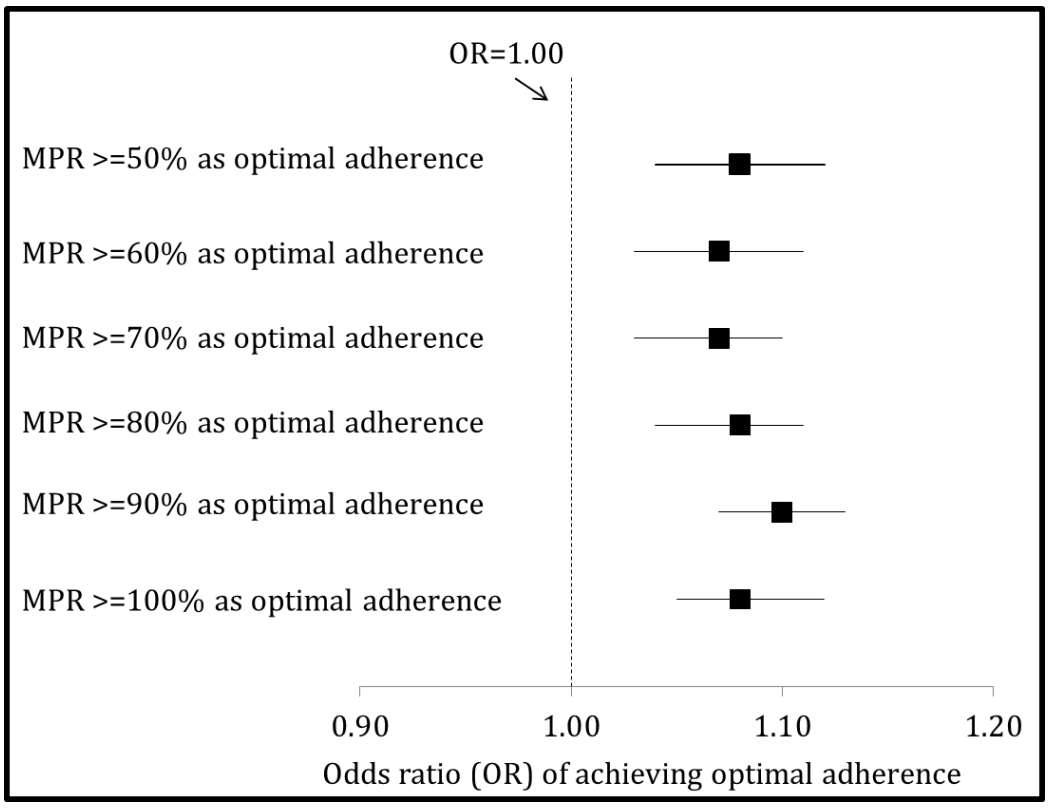
**Figure 4.11 Adjusted Odds Ratio of Achieving Optimal Adherence* Following Implementation of the Seniors' Drug Plan Stratified by Age.**




*Optimal adherence was defined as a Medication Possession Ratio ≥ 80%

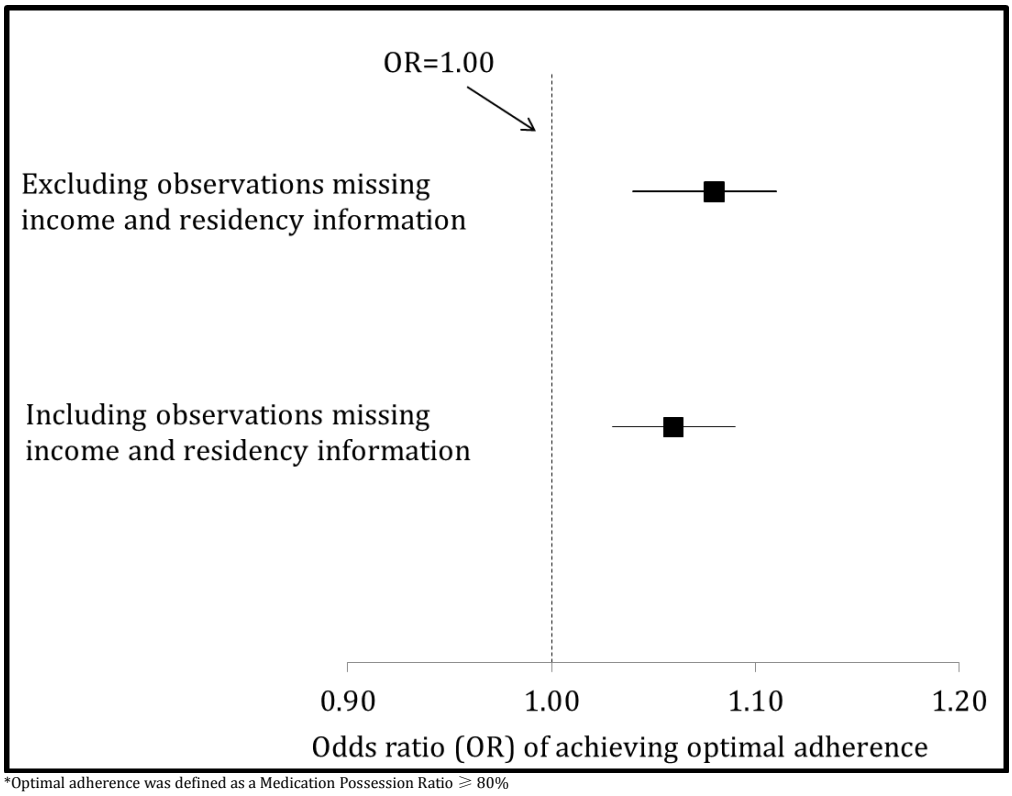
To test the influence of the threshold used to identify optimal adherence (i.e., MPR ≥80%), a sensitivity analysis was conducted with varying thresholds (MPR of 50% to 100%). Resulting odds ratios ranged from 1.07 to 1.10, without significant difference from the lowest threshold of MPR=50%, to the highest of 100% (Figure 4.12).

**Figure 4.12 Adjusted Odds Ratio of Achieving Specific Levels of Adherence Following Implementation of the Seniors' Drug Plan in Saskatchewan.**




In the original cohort development phase, 131,637 observations derived from 48,797 unique patients were excluded because of missing data for the estimation of residency and income. To determine if the exclusion of these observations impacted the generalizability of our results, the primary analysis was repeated after including all observations regardless of the availability of income level. The models were created using the same procedure except that the terms for income level were removed. Among this expanded cohort, the odds of achieving optimal adherence remained statistically significant following implementation of the SDP (Figure 4.13).

**Figure 4.13 Odds Ratio of Achieving Optimal Medication Adherence* Following Implementation of the SDP Among the Original Study Cohort and an Expanded Cohort Without Excluding Subjects with Missing Income level.**




*Optimal adherence was defined as a Medication Possession Ratio ⩾ 80%

One year following implementation of the SDP, a slight change to the process of eligibility was implemented on July 1st, 2008. Rather than a universal benefit, the SDP was restricted to seniors whose income did not exceed $75,480. To determine if this policy amendment impacted the benefit of the SDP, all 353,568 observations were examined. Among these, only 2,285 (0.6%) appeared to occur without the SDP coverage (i.e., out of pocket cost exceeded $15) following July 1st, 2008. We repeated the analysis by excluding these cases, and the results were consistent with the original/overall analysis.

# Chapter 5 Discussion

This retrospective study examined the impact of a drug benefit program for seniors in Saskatchewan (i.e., the SDP) where OOP costs for most prescription medications were capped at $15. In the two years following the launch of the SDP, government spending on medications increased by an average of $3.8 million per month (or 47.5%). This substantial investment was associated with a small (5.8%) increase in the total number of medications dispensed. Also, a small improvement in medication adherence was observed (OR 1.08; 95% CI 1.04 to 1.11) that was not consistently demonstrated in all drug classes or patient subgroups. Adherence was improved among patients receiving medications for blood-cholesterol-lowering or blood-pressure-lowering, but not among all patients receiving medications for diabetes or depression (i.e., only among subjects receiving metformin and SSRI). Also, adherence was improved among patients who had started their medication before the SDP was launched but not among those who received the SDP benefit on their very first dispensation.

The increase in total number of medication dispensations per month (5.8%) reached statistical significance; however, it was much smaller than the relative increase in government spending on medications over the same period (+47.5%). Consequently, it appears that the primary impact of the SDP was realized in cost savings to provincial beneficiaries who received their existing medications at the maximum cost of $15.

Although the reduced cost was undoubtedly perceived as a benefit to provincial residents, it did not appear to trigger a substantial change in the amount of medications consumed. These results are consistent with previous studies reporting average increases between 6-16% in medication use associated with patient cost reduction programs.(224–226)

The largest increase in overall use was observed with autonomic medications (+18.8%) and gastrointestinal drugs (+16.9%), while increases in other pharmacologic categories ranged between 1.4% and 8.1%. Increased use of autonomic medications was principally driven by the use of beta-agonist inhalers (e.g., salbutamol) for respiratory conditions while increases in gastrointestinal agents appeared to be driven by acid blocking medications (e.g., rabeprazole). Among the specific classes of chronic medications examined (i.e., blood-pressure-lowering, blood-cholesterol-lowering, blood-glucose-lowering agents, and antidepressant medications), increases were observed for all except blood-glucose-lowering agents. The finding of inconsistent impact on individual drug classes has also been reported by others. A systematic reviews by Polinski et al reported greater use in blood-pressure-lowering agents (+44%), and blood-cholesterol-lowering drugs (+22%), than in antidepressants (2%) following implementation of copayment plans in other jurisdictions.(227,228) The most likely explanation for a lack of impact on blood-glucose-lowering medications is the low cost oral agents such as metformin and glyburide, which accounted for 60% of the total number of dispensations in this class. Nearly half of the metformin and glyburide

dispensations cost $15 or less; thus the OOP costs for many patients did not change following the SDP launch (Figure 4.6).

The results of the medication adherence analysis followed a pattern very similar to the analysis of aggregate utilization (i.e., total number of dispensations). The SDP was associated with an increase in adherence to selected chronic medications for individuals ≥65 years of age while adherence among younger individuals (i.e., <65) did not change during this same period. Also, the SDP had no impact on adherence among patients receiving medications costing less than $15. Therefore, the improvement in medication adherence following the SDP implementation was not likely confounded by some unobserved factor affecting the entire population. Furthermore, poor medication adherence is known to be a multifactorial problem so the relatively small improvement associated with the SDP is consistent with our current understanding of the phenomenon. In other words, simply reducing one single factor (i.e., patient out of pocket cost) will not result in substantial improvement to overall adherence levels.(229) A similar finding was reported by Choudhry and colleagues who found that full coverage for medications resulted in a 5% increase in the percentage of patients with optimal adherence (i.e., from 39% to 44%).(68)

The SDP affected prevalent medication users but not incident users. Several possible reasons for these results can be theorized. First, adherence levels decline much faster among incident users.(45) Thus, it is possible that the relative importance of cost

may be smaller in the early phases of therapy, when numerous other adherence barriers such as tolerability, attitudes, beliefs, and knowledge may be more impactful. On the other hand, prevalent users witnessed a direct reduction in the cost of their medications following the SDP launch. Perhaps this obvious cost reduction motivated a slight improvement in adherence for the following year. Most importantly, this study was restricted to a one year period of adherence assessment so it is not known whether these small increases in adherence were sustained over the long term.

Previous research suggests that government investment on reducing patients' medication cost may have long-term benefits if adherence to chronic medications is improved. Patients with optimal adherence to blood-pressure-lowering, or blood-cholesterol-lowering medications can reduce risk of coronary artery disease events by 10%, or cerebrovascular events by 7-42%, compared to those with lower adherence.(37–39) Choudhry and colleagues found that a small improvement in adherence (i.e., 5% more adherent patients) was associated with 11% reduction in vascular events and revascularization procedures. The SDP in Saskatchewan appeared to have a smaller impact on adherence of around 2.3%. Thus, it is not clear whether this increase in adherence would be robust enough to impact health outcomes. Certainly, lower hospitalization rates for chronic conditions are expected to reduce health care costs and improve productivity.(68)

The evaluation of the SDP used comprehensive population based databases and produced results that were verified in sensitivity analyses. However, several limitations must be recognized. First, the presence of private medication coverage is not captured in Saskatchewan's health-administrative databases. Thus, we cannot be certain of the OOP costs paid by beneficiaries. However, rates of private insurance were not likely to have changed between seniors starting medications before versus after the SDP. Further, considering all individuals are over the age of 65, drug coverage from private insurance through employment is expected to be low. Secondly, the indicators of medication use are based on electronic refill databases, which are indirect measures of drug consumption. However, studies suggest that refill claims are highly concordant to actual intake.(230) Thirdly, only a one-year period of adherence was examined for individuals taking chronic medications. It is not clear whether the small impacts of the SDP would be sustained over a long-term follow-up period. Fourth, the impact of the SDP on medication adherence was restricted to a few classes of chronic medications only. Measurement of adherence to all types of medication classes would not be feasible. Moreover, many medication classes such as antibiotics and pain medications are not meant to be taken chronically. However, the medications examined in this study represented the most commonly used chronic medications in Canada and corresponded to the diseases of highest prevalence in elderly patients. In addition, an examination of all drugs was undertaken by the aggregate analysis of overall drug utilization. Lastly, we did not control for each individual's overall medication cost. Hypothetically, the benefit of the SDP may have been greater among seniors receiving multiple medications because

of greater savings on total medication costs. It would be interesting to conduct further analyses in this regard.

# Chapter 6 Conclusion

The SDP increased government drug spending in seniors by 47.5% following its launch on July 1st, 2007. This substantial investment into drug costs resulted in a small increase in overall drug utilization. Also, a statistically significant improvement in medication adherence was observed for specific chronic medications; however, it remains unknown if these small improvements have translated into health benefits and/or economic savings for downstream health care services.

The findings from this study indicate the SDP impact was not consistent across all drugs or types of medication users. A deeper understanding about the influence of cost-reduction strategies could be achieved if changes to the plan were implemented to specific subgroups such as prevalent users. Regardless, it is undeniable that seniors in Saskatchewan are the most frequent recipients of chronic medications; thus cost reduction for these individuals must have provided substantial relief independent of the impact on adherence and utilization.

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# Appendix A. Number of Observations in Stratified Analysis

| Stratification | Subgroups | Pre-SDP* | Post-SDP* |
|---|---|---|---|
| By age group | Age 65 and above | 62,759 | 83,950 |
| | Age 40-64 | 95,457 | 111,402 |
| By cost of medication | ≤$15 (a)* | 8,294 | 8,706 |
| | $16-30 (b)* | 8,307 | 13,180 |
| | >$30 (c)* | 93,498 | 102,876 |
| | *Covered by other benefit plans (d)* (excluded in this stratified analysis)* | *48,117* | *70,590* |
| By coverage of other benefit plans | Not covered by other benefit plans (i)* | 101,805 | 116,056 |
| | Covered by other benefit plans (ii)* | 4,437 | 66,369 |
| | *Cost per dispensation ≤$15(iii)* (excluded in this stratified analysis)* | *51,974* | *12,927* |
| By medication class | Statin | 43,899 | 58,056 |
| | ACEI/ARB* | 62,348 | 75,439 |
| | *CCB (excluded in this stratified analysis)** | *1,193* | *1,243* |
| | Metformin | 16,548 | 21,224 |
| | Glyburide | 6,742 | 6,783 |
| | SSRI* | 18,395 | 21,662 |
| | SNRI* | 9,091 | 10,945 |
| By user type | Incident users | 31,072 | 36,052 |
| | Prevalent users | 125,270 | 157,426 |
| | *Incident users that appeared in both periods (excluded in this stratified analysis)* | *1,874* | *1,874* |
| By age level | Age 40-64 | 95,457 | 111,402 |
| | Age 65-69 | 19,786 | 24,664 |
| | Age 70-74 | 18,219 | 22,538 |
| | Age 75-79 | 14,667 | 19,359 |
| | Age 80 and above | 10,087 | 17,389 |
| By sex | Male | 74,922 | 94,146 |
| | Female | 83,294 | 101,206 |

*SDP=seniors' Drug Plan; Subgroup (a)= observations not in subgroup (d), and with at least one dispensation of total cost ≤$15;Subgroup (b), observations exclusive in subgroup (a), (c), and (d); Subgroup(c)=observations not in subgroup(a), or (d), and with at least one dispensation of total cost > $30; Subgroup (d) = observations with at least one dispensation of which patient self-payment <$15; Subgroup (i)=observations exclusive in subgroup (ii) and (iii); Subgroup (ii)=observations not in subgroup (iii), and with at least one dispensation of which patient self-payment <$15; Subgroup (iii) = observations with at least one dispensation of total cost ≤$15; ACEI = angiotensin-converting-enzyme inhibitor; ARB= angiotensin receptor blocker; CCB=calcium channel blocker; SSRI=selective serotonin reuptake; SNRI= serotonin-norepinephrine reuptake inhibitors.